SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: Maassab, Hunein F Herlocher, Martha L
- (ii) TITLE OF INVENTION: Cold-adapted Influenza Virus
- (iii) NUMBER OF SEQUENCES: 40
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: Anna M Lewak
 - (B) STREET: 5445 Corporate Drive
 - (C) CITY: Troy
 - (D) STATE: MI
 - (E) COUNTRY: USA
 - (F) ZIP: 48098
 - (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
- (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER: US
 - (B) FILING DATE:
 - (C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:
 - (A) NAME: Lewak, Anna M
 - (B) REGISTRATION NUMBER: 33006

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O 3 1993

GROUP 1800

(C) REFERENCE/DOCKET NUMBER: 2115-00257

X/

(ix) TELECOMMUNICATION INFORMATION:

- (A) TELEPHONE: 313-641-1600
- (B) TELEFAX: 313-641-0270

(2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 890 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: cold-adapted "Master Strain" A/Ann Arbor/6/60 7PI (H2N2)
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: NS
- (ix) FEATURE:
 - (A) NAME/KEY: exon
 - (B) LOCATION: 27..56
 - (D) OTHER INFORMATION: /product= "nonstructural protein NS2" /gene= "NS" /note= "nonstructural protein NS2" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(483, "a")

61

(D) OTHER INFORMATION: /note= "a in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: exon
- (B) LOCATION: 529..861
- (D) OTHER INFORMATION: /product= "nonstructural protein NS2" /gene= "NS" /note= "nonstructural protein NS2" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(813, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: join(27..56, 529..861)
- (D) OTHER INFORMATION: /product= "nonstructural protein NS2" /gene= "NS" /note= "nonstructural protein NS2" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 27..677
- (D) OTHER INFORMATION: /product= "nonstructural protein NS1" /gene= "NS" /note= "nonstructural protein NS1" /citation= ([1][2])

(x) PUBLICATION INFORMATION:

| - 55 - |
|---|
| (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G |
| (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus |
| (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA |
| (G) DATE: 1993 |
| (K) RELEVANT RESIDUES IN SEQ ID NO:1: FROM 1 TO 890 |
| (x) PUBLICATION INFORMATION: |
| (A) AUTHORS: Cox, N J Kitame, F Kendal, A P Maassab, H F Naeve, C |
| (B) TITLE: Identification of sequence changes in the cold-adapted live attenuated influenza vaccine strain, A/Ann Arbor/6/60(H2N2) |
| (C) JOURNAL: Virology |
| (D) VOLUME: 167 |
| (F) PAGES: 554-567 |
| (G) DATE: 1988 |
| (K) RELEVANT RESIDUES IN SEQ ID NO:1: FROM 1 TO 890 |
| (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1: |
| AGCAAAAGCA GGGUGACAAA GACAUA AUG GAU CCU AAC ACU GUG UCA AGC UUU Met Asp Pro Asn Thr Val Ser Ser Phe 1 5 |
| CAG GUA GAU UGC UUC CUU UGG CAU GUC CGC AAA CAA GUU GCA GAC CAA Gln Val Asp Cys Phe Leu Trp His Val Arg Lys Gln Val Ala Asp Gln 10 15 20 25 |
| GAA CUA GGU GAU GCC CCA UUC CUU GAU CGG CUU CGC CGA GAU CAG AAG Glu Leu Gly Asp Ala Pro Phe Leu Asp Arg Leu Arg Arg Asp Gln Lys 30 35 40 |

UCC CUA AGG GGA AGA GGC AGU ACU CUC GGU CUG AAC AUC GAA ACA GCC Ser Leu Arg Gly Arg Gly Ser Thr Leu Gly Leu Asn Ile Glu Thr Ala 45 50 55 197

| | CGU Arg | | | | | | | | | | | | | | | 245 |
|-----|-------------------|-------|-------|-------------|-------|-------|-------|-------|-------|------|-----|-------|-------|-------|---------|-----|
| | GAG Glu 75 | | | | | | | | | | | | | | | 293 |
| | ACU Thr | | | | | | | | | | | | | | | 341 |
| | CCC Pro | | | | | | | | | | | | | | | 389 |
| | AUC Ile | | | | | | | | | | | | | | | 437 |
| | GAC Asp | | | | | | | | | | | | | | | 485 |
| | GCA Ala 155 | | | | | | | | | | | | | | | 533 |
| | AAU Asn | | | | | | | | | | | | | | | 581 |
| | UGG Trp | | | | | | | | | | | | | | | 629 |
| | UGG Trp | | | | | | | | | | | | | | | 677 |
| UAG | AAAC | GGA A | AAAU(| GCGA | AG AA | ACAAL | JUAG | G UCA | AAAA | GUUC | GAA | BAAAI | JAA (| SAUG | CUGAU | 737 |
| UGA | AGAAG | GUG A | AGACA | ACAAA | AU UG | SAAGA | NAAU | C AG | AGAAI | JAGU | UUU | GAGC | AAA (| JAACA | UAUUUAU | 797 |
| GCA | AGCCI | JUA (| CAGCI | JGCUA | אט טנ | JGAAG | SUGGA | A ACA | AAGA | SAUA | AGA | ACUUL | ncn (| CGUUL | JCAGCU | 857 |
| UAU | JUAAL | JGA (| JAAAA | NAAC | AC CO | CUUGL | JUUCL | J ACI | J | | | | | | | 890 |

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 217 amino acids

a1

- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Asp Pro Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp
1 5 10 15

His Val Arg Lys Gln Val Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe 20 25 30

Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser 35 40 45

Thr Leu Gly Leu Asn Ile Glu Thr Ala Thr Arg Val Gly Lys Gln Ile 50 55 60

Val Glu Arg Ile Leu Lys Glu Glu Ser Asp Glu Ala Leu Lys Met Thr 65 70 75 80

Met Ala Ser Ala Pro Ala Ser Arg Tyr Leu Thr Asp Met Thr Ile Glu 85 90 95

Glu Met Ser Arg Asp Trp Phe Met Leu Met Pro Lys Gln Lys Val Ala 100 105 110

Gly Pro Leu Cys Ile Arg Met Asp Gln Ala Ile Met Asp Lys Asn Ile 115 120 125

Ile Leu Lys Ala Asn Phe Ser Val Ile Phe Asp Arg Leu Glu Thr Leu 130 135 140

Ile Leu Leu Arg Ala Phe Thr Glu Thr Gly Ala Ile Val Gly Glu Ile 145 150 155 160

Ser Pro Leu Pro Ser Leu Pro Gly His Thr Asn Glu Asp Val Lys Asn 165 170 175

Ala Ile Gly Val Leu Ile Gly Gly Leu Glu Trp Asn Asp Asn Thr Val 180 185 190

Arg Val Ser Lys Thr Leu Gln Arg Phe Ala Trp Arg Ser Ser Asp Glu 195 200 205

Asn Gly Arg Pro Pro Leu Thr Pro Lys 210 215

(2) INFORMATION FOR SEQ ID NO:3:

ACA GAG AAU AGU UUU GAG CAA AUA ACA UUU AUG CAA GCC UUA CAG CUG Thr Glu Asn Ser Phe Glu Gln Ile Thr Phe Met Gln Ala Leu Gln Leu

100

95

90

341

CUA UUU GAA GUG GAA CAA GAG AUA AGA ACU UUC UCG UUU CAG CUU AUU Leu Phe Glu Val Glu Gln Glu Ile Arg Thr Phe Ser Phe Gln Leu Ile 115 UAAUGAUAAA AAACACCCUU GUUUCUACU (2) INFORMATION FOR SEQ ID NO:4: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 121 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4: Met Asp Pro Asn Thr Val Ser Ser Phe Gln Asp Ile Leu Met Arg Met 1 Ser Lys Met Gln Leu Gly Ser Ser Ser Glu Asp Leu Asn Gly Met Ile Thr Gln Phe Glu Ser Leu Lys Leu Tyr Arg Asp Ser Leu Gly Glu Ala Val Met Arg Met Gly Asp Leu His Ser Leu Gln Asn Arg Asn Gly Lys 50 Trp Arg Glu Gln Leu Gly Gln Lys Phe Glu Glu Ile Arg Trp Leu Ile Glu Glu Val Arg His Lys Leu Lys Ile Thr Glu Asn Ser Phe Glu Gln 90

- (2) INFORMATION FOR SEQ ID NO:5:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1027 base pairs

389

418

Ile Thr Phe Met Gln Ala Leu Gln Leu Leu Phe Glu Val Glu Gln Glu 110 100

Ile Arg Thr Phe Ser Phe Gln Leu Ile 115 120

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: cold-adapted "Master Strain" A/Ann Arbor/6/60 7PI (H2N2)
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: M
- (ix) FEATURE:
 - (A) NAME/KEY: exon
 - (B) LOCATION: 26..51
 - (D) OTHER INFORMATION: /product= "matrix protein M2" /gene= "M" /note= "matrix protein M2" /citation= ([1][2])
- (ix) FEATURE:
 - (A) NAME/KEY: exon
 - (B) LOCATION: 740..1004
 - (D) OTHER INFORMATION: /product= "matrix protein M2" /gene= "M" /note= "matrix protein M2" /citation= ([1][2])
- (ix) FEATURE:
 - (A) NAME/KEY: conflict
 - (B) LOCATION: replace(969, "u")
 - (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3)" /citation= ([1][2])

61

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: join(26..51, 740..1004)
- (D) OTHER INFORMATION: /product= "matrix protein M2" /gene= "M" /note= "matrix protein M2" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 26..781
- (D) OTHER INFORMATION: /product= "matrix protein M1" /gene= "M" /note= "matrix protein M1" /citation= ([1][2])

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G
- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA
- (G) DATE: 1993
- (K) RELEVANT RESIDUES IN SEQ ID NO:5: FROM 1 TO 1027

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Cox, N J
 Kitame, F
 Kendal, A P
 Maassab, H F
 Naeve, C
- (B) TITLE: Identification of sequence changes in the cold-adapted live attenuated influenza vaccine strain, A/Ann Arbor/6/60(H2N2)
- (C) JOURNAL: Virology

(D) VOLUME: 167

(F) PAGES: 554-557

(G) DATE: 1988

(K) RELEVANT RESIDUES IN SEQ ID NO:5: FROM 1 TO 1027

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

| AGCAAAAGCA GGUAGAUAUU GAAAG | | CUA ACC GAG GUC GA Leu Thr Glu Val G 5 | |
|---|-------------|--|--|
| UAC GUU CUC UCU AUC AUC CCG Tyr Val Leu Ser Ile Ile Pro 10 15 | | | |
| CAG AGA CUU GAA GAU GUC UUU Gln Arg Leu Glu Asp Val Phe 30 | | Asn Thr Asp Leu G | |
| CUC AUG GAA UGG CUA AAG ACA Leu Met Glu Trp Leu Lys Thr 45 | | | |
| GGG AUU UUG GGA UUU GUA UUC Gly Ile Leu Gly Phe Val Phe 60 | | | |
| CUG CAG CGU AGA CGC UUU GUC Leu Gln Arg Arg Arg Phe Val 75 80 | Gln Asn Ala | | |
| CCA AAU AAC AUG GAC AGA GCA Pro Asn Asn Met Asp Arg Ala 90 95 | | | |
| GAG AUA ACA UUC CAU GGG GCC Glu Ile Thr Phe His Gly Ala 110 | | Ala Leu Ser Tyr S | |
| GGU GCA CUU GCC AGU UGU AUG Gly Ala Leu Ala Ser Cys Met 125 | | | |
| GUG ACC ACU GAA GUG GUC UUA Val Thr Thr Glu Val Val Leu 140 | | | |
| AUU GCU GAC UCC CAG CAU AGG Ile Ala Asp Ser Gln His Arg 155 160 | Ser His Arg | | |

| | | | | | | | | | | | | | | ACU Thr | | 580 |
|------|------------|-------------------|-------------|------------|---------|---------|----------|-------|-------|-------------|------------|--------------|-------|-------------------|------------|------|
| | | | | | | | | | | | | | | GCA Ala 200 | | 628 |
| | | | | | | | | | | | | | | AUG Met | AGA Arg | 676 |
| | | | | | | | | | | | | | | GAU Asp | | 724 |
| | | | | | | | | | | | | | | AUG Met | | 772 |
| | UUC Phe | | UGA | CCCU | CUU (| GUUGI | JUGC(| CG CO | GAGU/ | AUCAU | J UG(| GAU (| CUUG | | | 821 |
| CACI | JUGAL | JAU I | JGUG | GAUU | CU - UC | GAUC | AUCUI | טטט נ | JUUCA | AAAU | GCAL | JUUA | JCG (| cuuci | JUUAAA | 881 |
| CAC | GUC | JGA A | AAAG | AGGG | cc u | JCUA | CGGA | A GG/ | AGUA | CCAG | AGU | CUAU | SAG (| GGAA | BAAUAU | 941 |
| CGA | AAGG | AAC A | AGCA | GAGU | GC U | GUGG | AUUCI | J GA | CGAU | AGUC | AUUI | JUGU | CAG | CAUA | SAGCUG | 1001 |
| GAGI | JAAA | AAA (| CUAC | CUUGI | JU U | CUACI | J | | | | | | | | | 1027 |
| (2) | INF | orma [.] | TION | FOR | SEQ | ID I | NO:6: | • | | | | , | | | | |
| | | (i) : | SEQUI | ENCE | CHAI | RACTI | ERIST | TICS | : | | | | | | | |
| | | . , | • |) LEI | | | | | | 5 | | | | | | |
| | | | | ,) TYI | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| | | | ָט |) TOI | -ULU | 31: | iiile | a f | | | | | | | | |
| | (- | ii) I | MOLE | CULE | TYP | E: p | rote | in | | | | | | | | |
| | | | | | DEC | ^ D T D | T T O NI | C = (| | NO. | - . | | | | | |

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Ile Pro
1 5 10 15

Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe
20 25 30

Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr 35 40 45

Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe 50 55 60

Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Phe Val 65 70 75 80

Gln Asn Ala Leu Asn Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala 85 90 95

Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala 100 105 110

Lys Glu Ile Ala Leu Ser Tyr Ser Ala Gly Ala Leu Ala Ser Cys Met 115 120 125

Gly Leu Ile Tyr Asn Arg Met Gly Ala Val Thr Thr Glu Val Val Leu 130 135 140

Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg 145 150 155 160

Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu 165 170 . 175

Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met 180 185 190

Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Gln 195 200 205

Ala Arg Gln Met Val Gln Ala Met Arg Val Ile Gly Thr His Pro Ser 210 215 220

Ser Ser Ala Gly Leu Lys Asn Asp Leu Leu Glu Asn Leu Gln Ala Tyr 225 230 235 240

Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys 245 250

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 339 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

41

| | (ii) MOLECULE TYPE: RNA (genomic) | |
|---|---|-----|
| (| (ix) FEATURE: | |
| | (A) NAME/KEY: CDS | |
| | (B) LOCATION: 26316 | |
| | (D) OTHER INFORMATION: /product= "Matrix M2" | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7: | |
| | AGCAAAAGCA GGUAGAUAUU GAAAG AUG AGU CUU CUA ACC GAG GUC GAA ACG Met Ser Leu Leu Thr Glu Val Glu Thr 1 5 | 52 |
| | CCU AUC AGA AAC GAA UGG GGG UGC AGA UGC AAC GAU UCA AGU GAC CCU Pro Ile Arg Asn Glu Trp Gly Cys Arg Cys Asn Asp Ser Ser Asp Pro 10 15 20 25 | 100 |
| | CUU GUU GUU GCC GCG AGU AUC AUU GGG AUC UUG CAC UUG AUA UUG UGG Leu Val Val Ala Ala Ser Ile Ile Gly Ile Leu His Leu Ile Leu Trp 30 35 40 | 148 |
| | AUU CUU GAU CAU CUU UUU UUC AAA UGC AUU UAU CGC UUC UUU AAA CAC Ile Leu Asp His Leu Phe Phe Lys Cys Ile Tyr Arg Phe Phe Lys His 45 50 55 | 196 |
| | GGU CUG AAA AGA GGG CCU UCU ACG GAA GGA GUA CCA GAG UCU AUG AGG Gly Leu Lys Arg Gly Pro Ser Thr Glu Gly Val Pro Glu Ser Met Arg 60 65 70 | 244 |
| | GAA GAA UAU CGA AAG GAA CAG CAG AGU GCU GUG GAU UCU GAC GAU AGU Glu Glu Tyr Arg Lys Glu Gln Gln Ser Ala Val Asp Ser Asp Asp Ser 75 80 85 | 292 |
| | CAU UUU GUC AGC AUA GAG CUG GAG UAAAAAACUA CCUUGUUUCU ACU His Phe Val Ser Ile Glu Leu Glu 90 95 | 339 |
| | (2) INFORMATION FOR SEQ ID NO:8: | |
| | (i) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 97 amino acids (B) TYPE: amino acid | |

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp Pro Leu Val Val Ala Ala Ser Ile 20 25 30

Ile Gly Ile Leu His Leu Ile Leu Trp Ile Leu Asp His Leu Phe Phe 35 40 45

Lys Cys Ile Tyr Arg Phe Phe Lys His Gly Leu Lys Arg Gly Pro Ser 50 55 60

Thr Glu Gly Val Pro Glu Ser Met Arg Glu Glu Tyr Arg Lys Glu Gln 65 70 75 80

Gln Ser Ala Val Asp Ser Asp Asp Ser His Phe Val Ser Ile Glu Leu 85 90 95

Glu

- (2) INFORMATION FOR SEQ ID NO:9:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1566 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: RNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: cold-adapted "Master Strain" A/Ann Arbor/6/60 7PI (H2N2)
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: NP

91

(ix) FEATURE:

- (A) NAME/KEY: mutation
- (B) LOCATION: replace(113, "c")
- (D) OTHER INFORMATION: /note= "c in ca "master" strain; a in wt2(3); a in 1988 reported ca vaccine strain (manuscript), but c reported in 1988 genbank" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(146, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(627, "c")
- (D) OTHER INFORMATION: /note= "c in ca "master" strain and in wt2(3); a in 1988 reported ca vaccine strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(909, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); c in 1988 reported ca vaccine strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1550, "a")
- (D) OTHER INFORMATION: /note= "a in ca "master" strain and in wt2(3)"

/citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 46..1539
- (D) OTHER INFORMATION: /product= "Nucleoprotein" /gene= "NP" /note= "nucleoprotein" /citation= ([1][2])

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R W
- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA
- (G) DATE: 1993
- (K) RELEVANT RESIDUES IN SEQ ID NO:9: FROM 1 TO 1566

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Cox, N J
 Kitame, F
 Kendal, A P
 Maassab, H F
 Naeve, C
- (B) TITLE: Identification of sequence changes in the cold-adapted live attenuated influenza vaccine strain, A/Ann Arbor/6/60 (H2N2)
- (C) JOURNAL: Virology
- (D) VOLUME: 167
- (F) PAGES: 554-567
- (G) DATE: 1988
- (K) RELEVANT RESIDUES IN SEQ ID NO:9: FROM 1 TO 1566

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

| AGCAAAAGCA GGGUAGAUAA UCACUCACUG AGUGACAUCA AAAUC AUG GCG UCC Met Ala Ser | | | | | | | | | | | | |
|---|-----------------|---|--|--|--|--|--|--|--|--|--|--|
| | | AUG GAA ACU GAU GGG GAA C Met Glu Thr Asp Gly Glu A 15 | | | | | | | | | | |
| | | GUC GGG AAG AUG AUU GGU G Val Gly Lys Met Ile Gly G 30 | | | | | | | | | | |
| | Ile Gln Met Cys | ACC GAA CUU AAA CUC AGU G Thr Glu Leu Lys Leu Ser A 45 50 | | | | | | | | | | |
| | | UUA ACA AUA GAG AGA AUG G Leu Thr Ile Glu Arg Met N 65 | | | | | | | | | | |
| | | AAA UAU CUG GAA GAA CAU C Lys Tyr Leu Glu Glu His F 80 | | | | | | | | | | |
| | | GGA GGA CCC AUA UAC AAG A Gly Gly Pro Ile Tyr Lys A 95 | | | | | | | | | | |
| | | GUC CUU UAU GAC AAA GAA G Val Leu Tyr Asp Lys Glu G 110 | | | | | | | | | | |
| | Arg Gln Ala Asn | AAU GGU GAU GAU GCA ACA G Asn Gly Asp Asp Ala Thr A 125 | | | | | | | | | | |
| | | UCC AAU UUG AAU GAU ACA A Ser Asn Leu Asn Asp Thr 1 145 | | | | | | | | | | |
| | | ACC GGA AUG GAU CCC AGG A Thr Gly Met Asp Pro Arg N 160 | | | | | | | | | | |
| | | CCU AGG AGG UCU GGA GCC G Pro Arg Arg Ser Gly Ala A 175 | | | | | | | | | | |
| | | AUG GUG AUG GAG UUG AUC A Met Val Met Glu Leu Ile A 190 | | | | | | | | | | |

| | | | | - | 70 | - | | | | |
|--|------|------|------|------|----|-------------------|--|-----|--|------|
| | | | | | | UUC Phe | | | | 678 |
| | | | | | | AUG Met | | | | 726 |
| | | | | | | AUG Met | | | | 774 |
| | | | | | | GAA Glu | | | | 822 |
| | | | | | | GUU Va1 270 | | | | 870 |
| | | | | | | GCC Ala | | | | 918 |
| | | | | | | GAC Asp | | | | 966 |
| | | | | | | CCG Pro | | Asn | | 1014 |
| | | | | | | AAU Asn | | | | 1062 |
| | | | | | | ACC Thr 350 | | | | 1110 |
| | | | | | | GCU Ala | | | | 1158 |
| | | | | | | AGA Arg | | | | 1206 |
| | | | | | | CAA Gln | | | | 1254 |
| | | | | | | GUG Val | | | | 1302 |
| | | | | | | | | | | |

| | | | | | | | | | | AAU Asn | | | 1350 |
|------|------|-------|------|------|------|-------|----|--|--|-------------------|--|--|------|
| | | | | | | | | | | AUG Met | | | 1398 |
| | | | | | | | | | | UUC Phe | | | 1446 |
| | | | | | | | | | | GAC Asp 480 | | | 1494 |
| | | | | | | | | | | UAC Tyr | | | 1539 |
| UAAG | GAA/ | AAA A | AUAC | CCUU | SU U | JCUA(| CU | | | | | | 1566 |

(2) INFORMATION FOR SEQ ID NO:10:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 498 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Gly Glu Arg Gln Asn Ala Thr Glu Ile Arg Ala Ser Val Gly Lys Met
20 25 30

Ile Gly Gly Ile Gly Arg Phe Tyr Ile Gln Met Cys Thr Glu Leu Lys 35 40 45

Leu Ser Asp Tyr Glu Gly Arg Leu Ile Gln Asn Ser Leu Thr Ile Glu 50 55 60

Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu 65 70 75 80

Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile

| | | | | | | | | - | 72 | - | | | | | |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Tyr | Lys | Arg | Val 100 | Asp | Gly | Lys | Trp | Met 105 | Arg | Glu | Leu | Val | Leu 110 | Tyr | As |
| Lys | Glu | Glu 115 | Ile | Arg | Arg | Ile | Trp 120 | Arg | Gln | Ala | Asn | Asn 125 | G1y | Asp | As |
| Ala | Thr 130 | Ala | Gly | Leu | Thr | His 135 | Met | Met | Ile | Trp | His 140 | Ser | Asn | Leu | As |
| Asp 145 | Thr | Thr | Tyr | Gln | Arg 150 | Thr | Arg | Ala | Leu | Va1 155 | Arg | Thr | G1y | Met | As 16 |
| Pro | Arg | Met | Cys | Ser 165 | Leu | Met | Gln | G1y | Ser 170 | Thr | Leu | Pro | Arg | Arg 175 | Se |
| Gly | Ala | A1 a | Gly 180 | Ala | Ala | Val | Lys | Gly 185 | Val | Gly | Thr | Met | Val 190 | Met | G1 |
| Leu | Ile | Arg 195 | Met | Ile | Lys | Arg | G1y 200 | Ile | Asn | Asp | Arg | Asn 205 | Phe | Trp | Ar |
| Gly | Glu 210 | Asn | Gly | Arg | Lys | Thr 215 | Arg | Asn | Ala | Tyr | G1u 220 | Arg | Met | Cys | As |
| Ile 225 | Leu | Lys | Gly | Lys | Phe 230 | Gln | Thr | Ala | Ala | G1n 235 | Arg | Ala | Met | Met | As 24 |
| G1n | Va1 | Arg | G1u | Ser 245 | Arg | Asn | Pro | Gly | Asn 250 | Ala | G1 u | Ile | G1u | Asp 255 | Le |
| Ile | Phe | Leu | A1a 260 | Arg | Ser | Ala | Leu | I1e 265 | Leu | Arg | G1y | Ser | Va1 270 | Ala | Hi |
| Lys | Ser | Cys 275 | Leu | Pro | Ala | Cys | Va1 280 | Tyr | G1y | Pro | Ala | Va1 285 | Ala | Ser | G1; |
| Tyr | Asp 290 | Phe | G1 u | Lys | G1u | G1y 295 | Tyr | Ser | Leu | Va1 | Gly 300 | Ile | Asp | Pro | Ph |
| Lys 305 | Leu | Leu | Gln | Asn | Ser 310 | Gln | Val | Tyr | Ser | Leu 315 | Ile | Arg | Pro | Asn | G1: |
| Asn | Pro | Ala | His | Lys 325 | Ser | Gln | Leu | Val | Trp 330 | Met | Ala | Cys | Asn | Ser 335 | A 1 |
| Ala | Phe | Glu | Asp 340 | Leu | Arg | Val | Ser | Ser | Phe | Ile | Arg | Gly | Thr | Lys | ۷a |

Ile Pro Arg Gly Lys Leu Ser Thr Arg Gly Val Gln Ile Ala Ser Asn 355 360 365

Glu Asn Met Asp Thr Met Gly Ser Ser Thr Leu Glu Leu Arg Ser Arg 370 375 380

al

Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Asn Gln Gln Arg 385 390 395 400

Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg 405 410 415

Asn Leu Pro Phe Asp Lys Pro Thr Ile Met Ala Ala Phe Thr Gly Asn 420 425 430

Ala Glu Gly Arg Thr Ser Asp Met Arg Ala Glu Ile Ile Arg Met Met 435 440 445

Glu Gly Ala Lys Pro Glu Glu Val Ser Phe Gln Gly Arg Gly Val Phe 450 455 460

Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp 465 470 475 480

Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Tyr 485 490 495

Asp Asn

- (2) INFORMATION FOR SEQ ID NO:11:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2233 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: RNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: cold-adapted "Master Strain" A/Ann Arbor/6/60 7PI (H2N2)
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: PA
 - (ix) FEATURE:
 - (A) NAME/KEY: conflict

- (B) LOCATION: replace(20, "c")
- (D) OTHER INFORMATION: /note= "c in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(75, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); u in 1988 reported ca vaccine strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1861, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(2167..2168, "cc")
- (D) OTHER INFORMATION: /note= "cc in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 25..2172
- (D) OTHER INFORMATION: /product= "polymerase acidic protein" /gene= "PA" /note= "polymerase acidic protein" /citation= ([1][2])

(x) PUBLICATION INFORMATION:

| (A) | AUTHORS: Herlocher, M L Maassab, H F Webster, R G |
|----------------|---|
| (B) | TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus |
| (C) | JOURNAL: Proceedings of the National Academy of Sciences of the USA |
| (G) | DATE: 1993 |
| (K) | RELEVANT RESIDUES IN SEQ ID NO:11: FROM 1 TO 2233 |
| (x) PUBL | ICATION INFORMATION: |
| (A) | AUTHORS: Cox, N J Kitame, F Kendal, A P Maassab, H F Naeve, C |
| (B) | TITLE: Identification of sequence changes in the cold-adapted live attenuated influenza strain, A/Ann Arbor/6/60(H2N2) |
| (C) | JOURNAL: Virology |
| (D) | VOLUME: 167 |
| (F) | PAGES: 554-567 |
| (G) | DATE: 1988 |
| (K) | RELEVANT RESIDUES IN SEQ ID NO:11: FROM 1 TO 2233 |
| (xi) SEQUE | ENCE DESCRIPTION: SEQ ID NO:11: |
| AGCGAAAGCA GGU | JACUGAUC CGAA AUG GAA GAU UUU GUG CGA CAA UGC UUC Met Glu Asp Phe Val Arg Gln Cys Phe 1 5 |
| | JU GUC GAG CUU GCG GAA AAA GCA AUG AAA GAG UAU GGA 99 le Val Glu Leu Ala Glu Lys Ala Met Lys Glu Tyr Gly 15 20 25 |
| | AA AUC GAA ACA AAC AAA UUU GCA GCA AUA UGC ACU CAC ys Ile Glu Thr Asn Lys Phe Ala Ala Ile Cys Thr His 30 35 40 |
| Leu Glu Val Cy | GC UUC AUG UAU UCA GAU UUU CAU UUC AUC AAU GAG CAA 195 vs Phe Met Tyr Ser Asp Phe His Phe Ile Asn Glu Gln 50 55 |

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GGC GAG UCA AUA AUA GUA GAG CUU GAU GAU CCA AAU GCA CUU UUG AAG 243 Gly Glu Ser Ile Ile Val Glu Leu Asp Asp Pro Asn Ala Leu Leu Lys CAC AGA UUU GAA AUA AUA GAG GGA AGA GAU CGC ACA AUG GCC UGG ACA 291 His Arg Phe Glu Ile Ile Glu Gly Arg Asp Arg Thr Met Ala Trp Thr 80 GUA GUA AAC AGU AUU UGC AAC ACU ACA GGA GCU GAG AAA CCG AAG UUU 339 Val Val Asn Ser Ile Cys Asn Thr Thr Gly Ala Glu Lys Pro Lys Phe 90 95 CUG CCA GAU UUG UAU GAU UAC AAG GAG AAU AGA UUC AUC GAG AUU GGA 387 Leu Pro Asp Leu Tyr Asp Tyr Lys Glu Asn Arg Phe Ile Glu Ile Gly 110 115 120 GUG ACA AGG AGG GAA GUC CAC AUA UAC UAU CUU GAA AAG GCC AAU AAA 435 Val Thr Arg Arg Glu Val His Ile Tyr Tyr Leu Glu Lys Ala Asn Lys 125 130 AUU AAA UCU GAG AAG ACA CAC AUC CAC AUU UUC UCA UUC ACU GGG GAA 483 Ile Lys Ser Glu Lys Thr His Ile His Ile Phe Ser Phe Thr Gly Glu 145 GAA AUG GCC ACA AAG GCC GAC UAC ACU CUC GAU GAG GAA AGC AGG GCU 531 Glu Met Ala Thr Lys Ala Asp Tyr Thr Leu Asp Glu Glu Ser Arg Ala 155 160 AGG AUC AAA ACC AGA CUA UUC ACC AUA AGA CAA GAA AUG GCU AGC AGA 579 Arg Ile Lys Thr Arg Leu Phe Thr Ile Arg Gln Glu Met Ala Ser Arg 170 185 175 180 GGC CUC UGG GAU UCC UUU CAU CAG UCC GAA AGA GGC GAA GAA ACA AUU 627 Gly Leu Trp Asp Ser Phe His Gln Ser Glu Arg Gly Glu Glu Thr Ile 190 200 GAA GAA AGA UUU GAA AUC ACA GGG ACA AUG CGC AGG CUC GCC GAC CAA 675 Glu Glu Arg Phe Glu Ile Thr Gly Thr Met Arg Arg Leu Ala Asp Gln 205 AGU CUC CCG CCG AAC UUC UCC UGC CUU GAG AAU UUU AGA GCC UAU GUG 723 Ser Leu Pro Pro Asn Phe Ser Cys Leu Glu Asn Phe Arg Ala Tyr Val 225 GAU GGA UUC GAA CCG AAC GGC UAC AUU GAG GGC AAG CUU UCU CAA AUG 771 Asp Gly Phe Glu Pro Asn Gly Tyr Ile Glu Gly Lys Leu Ser Gln Met 245 235 819 UCC AAA GAA GUA AAU GCU AAA AUU GAA CCU UUU CUG AAA ACA ACA CCA Ser Lys Glu Val Asn Ala Lys Ile Glu Pro Phe Leu Lys Thr Thr Pro 260 250 255 265 AGA CCA AUU AGA CUU CCG GAU GGG CCU CCU UGU UCU CAG CGG UCC AAA 867 Arg Pro Ile Arg Leu Pro Asp Gly Pro Pro Cys Ser Gln Arg Ser Lys 270 280

| | | AUG Met 285 | | | | | | | | 915 |
|---|---|-------------------|---|------|------|------|------|------|--|------|
| _ | - | GGA Gly | _ | | | | | | | 963 |
| | | UGG Trp | | | | | | | | 1011 |
| | | AAU Asn | | | | | | | | 1059 |
| | | GAG Glu | | | | | | | | 1107 |
| | | CAG G1n 365 | | | | | | | | 1155 |
| | | UUU Phe | | | | | | | | 1203 |
| | | GAA Glu | | | | | | | | 1251 |
| | | AAĠ Lys | | | | | | | | 1299 |
| | | GGA Gly | | | | | | | | 1347 |
| | | UAC Tyr 445 | | | | | | | | 1395 |
| | | AAG Lys | | | | | | | | 1443 |
| | | AUG Met | | | | | | | | 1491 |
| | | GAG Glu | | | | | | | | 1539 |

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| | GGA G1y | | | | | | | | | | | | | , | 1587 |
|---|-------------------|------|-------|------|------|-------|-------|-------|-------|-----|-------|------|--|---|------|
| | AUG Met | | | | | | | | | | | | | | 1635 |
| | AAG. Lys | | | | | | | | | | | | | | 1683 |
| | GGC G1y 555 | | | | | | | | | | | | | | 1731 |
| - | UCA Ser | | | | | _ | | | | | | | | | 1779 |
| | CAG Gln | | | | | | | | | | | | | | 1827 |
| | AAG Lys | | | | | | | | | | | | | | 1875 |
| | UGG Trp | | | | | | | | | | | | | | 1923 |
| | AAG Lys 635 | | | | | | | | | | | | | | 1971 |
| | GCA Ala | | | | | | | | | | | | | | 2019 |
| | CUU Leu | | | | | | | | | | | | | | 2067 |
| | CUU Leu | | | | | | | | | | | | | | 2115 |
| | UGG Trp | | | | | | | | | | | | | | 2163 |
| | CCA Pro 715 | UAGU | JUGUG | GC A | AUGO | CUACU | JA UL | JUGCL | JAUCO | AUA | ACUGL | JCCA | | | 2212 |

(2) INFORMATION FOR SEQ ID NO:12:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 716 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Met Glu Asp Phe Val Arg Gln Cys Phe Asn Pro Met Ile Val Glu Leu
1 5 10 15

Ala Glu Lys Ala Met Lys Glu Tyr Gly Glu Asp Leu Lys Ile Glu Thr 20 25 30

Asn Lys Phe Ala Ala Ile Cys Thr His Leu Glu Val Cys Phe Met Tyr 35 40 45

Ser Asp Phe His Phe Ile Asn Glu Gln Gly Glu Ser Ile Ile Val Glu 50 55 60

Leu Asp Asp Pro Asn Ala Leu Leu Lys His Arg Phe Glu Ile Ile Glu 65 70 75 80

Gly Arg Asp Arg Thr Met Ala Trp Thr Val Val Asn Ser Ile Cys Asn 85 90 95

Thr Thr Gly Ala Glu Lys Pro Lys Phe Leu Pro Asp Leu Tyr Asp Tyr 100 105 110

Lys Glu Asn Arg Phe Ile Glu Ile Gly Val Thr Arg Arg Glu Val His
115 120 125

Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His 130 135 140

Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp 145 150 155 160

Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe 165 170 175

Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe His 180 185 190 W

Gin Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr Gly Thr Met Arg Arg Leu Ala Asp Gln Ser Leu Pro Pro Asn Phe Ser Cys Leu Glu Asn Phe Arg Ala Tyr Val Asp Gly Phe Glu Pro Asn Gly 230 Tyr Ile Glu Gly Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Lys 250 Ile Glu Pro Phe Leu Lys Thr Thr Pro Arg Pro Ile Arg Leu Pro Asp 260 265 Gly Pro Pro Cys Ser Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu 280 Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu Tyr Asp Ala Ile Lys Cys Met Arg Thr Phe Phe Gly Trp Lys Glu Pro Tyr Val Val Lys Pro His Glu Lys Gly Ile Asn Pro Asn Tyr Leu Leu 325 330 335 Ser Trp Lys Gln Val Leu Ala Glu Leu Gln Asp Ile Glu Asn Glu Glu Lys Ile Pro Arg Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp 360 Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Asp Asp Cys 370 375 380 Arg Asp Val Ser Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Leu 385 390 Arg Ser Leu Ser Ser Trp Ile Gln Asn Glu Phe Asn Lys Ala Cys Glu 410 Leu Thr Asp Ser Ile Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val 420 430 Ala Pro Ile Glu His Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala Glu Val Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Asp Phe 465 470 475 480 Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg

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Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg 510 500 505 Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr 520 Asp Pro Arg Leu Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu 535 Ile Gly Asp Met Leu Leu Arg Ser Ala Ile Gly Gln Val Ser Arg Pro 560 545 550 555 Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys 570 Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile 585 Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr 595 600 605 Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser 615 Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Val Val Gln Ala Leu 665 Arg Asp Asn Leu Glu Pro Gly Thr Phe Asp Leu Gly Gly Leu Tyr Glu 680 Ala Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala 690 695 700 Ser Trp Phe Asn Ser Phe Leu Thr His Ala Pro Arg 705 710 715!

(2) INFORMATION FOR SEQ ID NO:13:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2341 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

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- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: cold adapted "Master Strain" A/AA/6/60 7PI (H2N2)
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: PB1
- (ix) FEATURE:
 - (A) NAME/KEY: conflict
 - (B) LOCATION: replace(123, "g")
 - (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3)" /citation= ([1][2])
- (ix) FEATURE:
 - (A) NAME/KEY: conflict
 - (B) LOCATION: replace(486, "u")
 - (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3)" /citation= ([1][2])
- (ix) FEATURE:
 - (A) NAME/KEY: conflict
 - (B) LOCATION: replace(1195, "g")
 - (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3)" /citation= ([1][2])
- (ix) FEATURE:
 - (A) NAME/KEY: mutation
 - (B) LOCATION: replace(1276, "g")

(D) OTHER INFORMATION: /note= "g in ca "master" strain; a in wt2(3); g in 1988 reported ca vaccine strain"
/citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1395, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1766, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(2005, "a")
- (D) OTHER INFORMATION: /note= "a in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(2019, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 25..2295

| (D) | OTHER INFORMATION: /product= "polymerase basic 1" /gene= "PB1" /note= "polymerase basic 1" /citation= ([1][2]) | |
|--------------|--|-----------|
| (x) PUBL | LICATION INFORMATION: | |
| (A) | AUTHORS: Herlocher, M L Maassab, H F Webster, R G | |
| (B) |) TITLE: Molecular and biological changes in the cold ada master strain A/AA/6/60 (H2N2) influenza virus | pted |
| (c) |) JOURNAL: Proceedings of the National Academy of Science the USA | s of |
| (G) |) DATE: 1993 | |
| (K) | RELEVANT RESIDUES IN SEQ ID NO:13: FROM 1 TO 2341 | |
| (x) PUBL | LICATION INFORMATION: | |
| (A) | AUTHORS: Cox, N J Kitame, F Kendal, A P Maassab, H F Naeve, C | |
| (B) |) TITLE: Identification of sequence changes in the cold-a | dapted |
| (C) |) JOURNAL: Virology | |
| (D) | VOLUME: 167 | |
| (F) | PAGES: 554-567 | |
| (G) | DATE: 1988 | |
| (K) | RELEVANT RESIDUES IN SEQ ID NO:13: FROM 1 TO 2341 | |
| (xi) SFOU | JENCE DESCRIPTION: SEQ ID NO:13: | |
| | GCAAACCAU UUGA AUG GAU GUC AAU CCG ACC UUA CUU UUC | 51 |
| ndcunnach du | Met Asp Val Asn Pro Thr Leu Leu Phe 1 5 | J1 |
| | CCA GCG CAA AAU GCC AUA AGU ACU ACA UUC CCU UAU ACU Pro Ala Gln Asn Ala Ile Ser Thr Thr Phe Pro Tyr Thr 15 20 25 | 99 |

| | | | CAU His | | | | | | 147 |
|--|--|--|-------------------|--|-----|--|--|--|-----|
| | | | CAA G1n | | Glu | | | | 195 |
| | | | CAC His | | | | | | 243 |
| | | | AGU Ser 80 | | | | | | 291 |
| | | | GAA Glu | | | | | | 339 |
| | | | GAA Glu | | | | | | 387 |
| | | | ACC Thr | | | | | | 435 |
| | | | GCC Ala | | | | | | 483 |
| | | | UCG Ser 160 | | | | | | 531 |
| | | | AAA Lys | | | | | | 579 |
| | | | AGA Arg | | | | | | 627 |
| | | | AAG Lys | | | | | | 675 |
| | | | UUG Leu | | | | | | 723 |
| | | | GCA Ala 240 | | | | | | 771 |

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| | | | | | | | UGU Cys | | 819 |
|--|--|--|--|--|---|--|-------------------|--|------|
| | | | | | | | AAG Lys | | 867 |
| | | | | | | | GAC Asp 295 | | 915 |
| | | | | | | | GAG Glu | | 963 |
| | | | | | | | AGA Arg | | 1011 |
| | | | | | | | AUG Met | | 1059 |
| | | | | | | | AGC Ser | | 1107 |
| | | | | | | | AGU Ser 375 | | 1155 |
| | | | | | | | GAA Glu | | 1203 |
| | | | | | | | AUG Met | | 1251 |
| | | | | | | | AUC Ile | | 1299 |
| | | | | | - | | GAC Asp | | 1347 |
| | | | | | | | AAU Asn 455 | | 1395 |
| | | | | | | | AAG Lys | | 1443 |

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| | | | AAG Lys 480 | | | | | | | 1491 |
|--|---|--|-------------------|---|---|---|--|------|--|------|
| | | | UUC Phe | | - | | | | | 1539 |
| | | | UUU Phe | | | | | | | 1587 |
| | | | ACA Thr | | | | | | | 1635 |
| | - | | GCC Ala | - | | - | | | | 1683 |
| | | | CGG Arg 560 | | | | | | | 1731 |
| | | | CUA Leu | | | | | | | 1779 |
| | | | UCG Ser | | | | | | | 1827 |
| | | | GAA Glu | | | | | | | 1875 |
| | | | CUU Leu | | | | | | | 1923 |
| | | | GUA Val 640 | | | | | | | 1971 |
| | | | GAA Glu | | | | | | | 2019 |
| | | | CGC Arg | | | | | | | 2067 |
| | | | AUG Met | | | | | | | 2115 |

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|-----------|-----------|------------|-----------|-----------|-----------|-----------|-------------------|-----------|-------------------|-----------|-----------|-----------|-----------|-----------|-----------|------|
| | | | | | | | | | AGA Arg | | | | | | | 2163 |
| | | | | | | | | | CGG Arg | | | | | | | 2211 |
| | | | | | | | | | GAG Glu | | | | | | | 2259 |
| | | | | | | | | | CGG Arg 755 | | | UAGI | JGAAI | JUU | | 2305 |
| AGC | JUGU | ccu ı | JCAUG | SAAA | AA AI | JGCCI | JUGUI | J UCI | JACU | | | | | | | 2341 |
| | | | | | | | | | | | | | | | | |
| (2) | INFO | ORMA | LION | FOR | SEQ | ID I | NO:14 | 4: | | | | | | | | |
| | 1 | (i) : | SEQUE | ENCE | CHAI | RACTI | ERIS | TICS | : | | | | | | | |
| | | | (A) |) LEI | NGTH: | : 757 | 7 am | ino a | acids | 5 | | | | | | |
| | | | (B) |) TYI | PE: a | amino | ac. | i d | | | | | | | | |
| | | | (D) |) TO | OL00 | GY: | linea | ar | | | | | | | | |
| | (- | ii) M | 40LE(| CULE | TYPI | E: pı | rote [.] | in | | | | | | | | |
| | () | ci) S | SEQUE | ENCE | DES | CRIP | TION: | : SEC | Q ID | NO: | 14: | | | | | |
| | • | | Asn | | | | | | Leu 10 | - | | | | | Asn | |
| Ala | Ile | Ser | Thr 20 | Thr | Phe | Pro | Tyr | Thr 25 | Gly | Asp | Pro | Pro | Tyr 30 | Ser | His | |
| Gly | Thr | G1 y 35 | Thr | G1y | Tyr | Thr | Met 40 | Asp | Thr | Val | Asn | Arg 45 | Thr | His | Gln | |
| Tyr | Ser 50 | G1 u | Lys | Gly | Lys | Trp 55 | Thr | Thr | Asn _. | Thr | G1u 60 | Thr | Gly | Ala | His | |
| G1n 65 | Leu | Asn | Pro | Ile | Asp 70 | Gly | Pro | Leu | Pro | G1u 75 | Asp | Asn | Glu | Pro | Ser 80 | |
| Gly | Tyr | Ala | G1n | Thr 85 | Asp | Cys | Val | Leu | G1 u 90 | Ala | Met | Ala | Phe | Leu 95 | Glu | |
| | | | | | | | | | | | | | | | | |

Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu

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| | | | 100 | | | | | 103 | | | | | 110 | | |
|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Val · | Ile | Gln 115 | Gln | Thr | Arg | Val | Asp 120 | Lys | Leu | Thr | Gln | Gly 125 | Arg | Gln | Thr |
| Tyr | Asp 130 | Trp | Thr | Leu | Asn | Arg 135 | Asn | G1n | Pro | Ala | Ala 140 | Thr | Ala | Leu | Alá |
| Asn 145 | Thr | Ile | G1u | Val | Phe 150 | Arg | Ser | Asn | G1 y | Leu 155 | Thr | Ala | Asn | Glu | Ser 160 |
| Gly | Arg | Leu | Ile | Asp 165 | Phe | Leu | Lys | Asp | Va1 170 | Ile | G1 u | Ser | Met | Asp 175 | Lys |
| G1u | Glu | Met | Glu 180 | Ile | Thr | Thr | His | Phe 185 | G1 n | Arg | Lys | Arg | Arg 190 | Val | Arg |
| Asp | Asn | Met 195 | Thr | Lys | Lys | Met | Va1 200 | Thr | Gln | Arg | Thr | Ile 205 | Gly | Lys | Lys |
| Lys | Gln 210 | Arg | Leu | Asn | Lys | Arg 215 | Ser | Tyr | Leu | Ile | Arg 220 | Ala | Leu | Thr | Leu |
| Asn 225 | Thr | Met | Thr | Lys | Asp 230 | Ala | G1 u | Arg | Gly | Lys 235 | Leu | Lys | Arg | Arg | A1 a |
| Ile | Ala | Thr | Pro | Gly 245 | Met | Gln | Ile | Arg | Gly 250 | Phe | Val | Tyr | Phe | Va1 255 | G1 u |
| Thr | Leu | Ala | Arg 260 | Ser | Ile | Cys | G1 u | Lys 265 | Leu | G1 u | Gln | Ser | G1y 270 | Leu | Pro |
| Val | Gly | G1y 275 | Asn | G1u | Lys | Lys | A1 a 280 | Lys | Leu | Ala | Asn | Va1 285 | Val | Arg | Lys |
| Met | Met 290 | Thr | Asn | Ser | Gln | Asp 295 | Thr | G1 u | Leu | Ser | Phe 300 | Thr | Ile | Thr | G1) |
| Asp 305 | Asn | Thr | Lys | Trp | Asn 310 | G1u | Asn | Gln | | Pro 315 | Arg | Met | Phe | Leu | A1 a |
| Met | Ile | Thr | Tyr | Ile 325 | Thr | Arg | Asn | Gln | Pro 330 | G1 u | Trp | Phe | Arg | Asn 335 | Val |
| Leu | Ser | Ile | A1a 340 | Pro | Ile | Met | Phe | Ser 345 | Asn | Lys | Met | Ala | Arg 350 | Leu | G1) |
| Lys | Gly | Tyr 355 | Met | Phe | Lys | Ser | Lys 360 | Ser | Met | Lys | Leu | Arg 365 | Thr | G1n | Πe |
| Pro | A1a 370 | G1u | Met | Leu | Ala : | Ser 375 | Ile | Asp | Leu | Lys | Tyr 380 | Phe | Asn | Glu | Ser |
| Thr 385 | Arg | Lys | Lys | Ile | G1u 390 | Glu | Ile | Arg | Pro | Leu 395 | Leu | Ile | Asp | Gly | Thr 400 |

Val Ser Leu Ser Pro Gly Met Met Gly Met Phe Asn Met Leu Ser Thr Val Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Lys Lys Tyr Thr 425 Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala Leu Ile Val Asn Ala Pro Asn His Asp Gly Ile Gln Ala Gly Val Asp 450 Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe 490 Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe 505 500 Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr 520 Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala 530 540 Gln Leu Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg 550 Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu 570 Lys Lys Leu Trp Gly Gln Thr Arg Ser Lys Ala Gly Leu Leu Val Ser 580 Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu 600 Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Gln Gly Arg Leu 620 Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val 625 640 Asn Asn Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu 645 Tyr Asp Ala Val Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg 665 Ser Ile Leu Asn Thr Ser Gln Arg Gly Ile Leu Glu Asp Glu Gln Met 675 680 685

Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser

690

695

700

Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser 705 710 715 720

Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys
725 730 735

Lys Glu Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu 740 745 750

Leu Arg Arg Gln Lys 755

(2) INFORMATION FOR SEQ ID NO:15:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2341 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: cold-adapted "Master Strain" A/Ann Arbor/6/60 7PI (H2N2)
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: PB2
- (ix) FEATURE:
 - (A) NAME/KEY: mutation
 - (B) LOCATION: replace(141, "g")
 - (D) OTHER INFORMATION: /note= "g in ca "master" strain; a in wt2(3); g in 1988 reported ca vaccine strain"
 /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(426, "c")
- (D) OTHER INFORMATION: /note= "c in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(714, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3); c in 1988 reported ca vaccine strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(821, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(963, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported ca vaccine strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1182, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3)" /citation= ([1][2])

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(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1212, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1353, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1923, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3)" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: mutation
- (B) LOCATION: replace(1933, "c")
- (D) OTHER INFORMATION: /note= "c in ca "master" strain; u in wt2(3); u in 1988 reported ca vaccine strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 28..2304
- (D) OTHER INFORMATION: /product= "polymerase basic 2" /gene= "PB2" /note= "polymerase basic 2" /citation= ([1][2])

| (x) PUBLICATION INFORMATION: | |
|---|---------|
| (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G | |
| (B) TITLE: Molecular and biological changes in the cold ada master strain A/AA/6/60 (H2N2) influenza virus | apted |
| (C) JOURNAL: Proceedings of the National Academy of Science the USA | es of |
| (G) DATE: 1993 | |
| (K) RELEVANT RESIDUES IN SEQ ID NO:15: FROM 1 TO 2341 | |
| (x) PUBLICATION INFORMATION: | |
| (A) AUTHORS: Cox, N J Kitame, F Kendal, A P Maassab, H F Naeve, C | |
| (B) TITLE: Identification of sequence changes in the cold-a live attenuated influenza vaccine strain, A/Ann Arbor/6/60(H2N2) | adapted |
| (C) JOURNAL: Virology | |
| (D) VOLUME: 167 | |
| (F) PAGES: 554-567 | |
| (G) DATE: 1988 | |
| (K) RELEVANT RESIDUES IN SEQ ID NO:15: FROM 1 TO 2341 | • |
| (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15: | |
| AGCGAAAGCA GGUCAAUUAU AUUCAAU AUG GAA AGA AUA AAA GAA CUA CGG Met Glu Arg Ile Lys Glu Leu Arg 1 5 | 51 |
| AAU CUG AUG UCG CAG UCU CGC ACU CGC GAG AUA CUA ACA AAA ACC ACA Asn Leu Met Ser Gln Ser Arg Thr Arg Glu Ile Leu Thr Lys Thr Thr 10 15 20 | 99 |
| GUG GAC CAU AUG GCC AUA AUU AAG AAG UAC ACA UCA GGG AGG CAG GAA Val Asp His Met Ala Ile Ile Lys Lys Tyr Thr Ser Gly Arg Gln Glu 25 30 35 40 | 147 |
| AAG AAC CCG UCA CUU AGG AUG AAA UGG AUG AUG GCA AUG AAA UAU CCG | 195 |

| Lys | Asn | Pro | Ser | Leu 45 | Arg | Met | Lys | Trp | Met 50 | Met | Ala | Met | Lys | Tyr 55 | Pro | |
|-----|-------------------|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|
| | ACA Thr | | | | | | | | | | | | | | | 243 |
| | GGG Gly | | | | | | | | | | | | | | | 291 |
| | AUG Met 90 | | | | | | | | | | | | | | | 339 |
| | ACA Thr | | | | | | | | | | | | | | | 387 |
| | GUC Val | | | | | | | | | | | | | | | 435 |
| | CAA G1n | | | | | | | | | | | | | | | 483 |
| | CUC Leu | | | | | | | | | | | | | | | 531 |
| | AAC Asn 170 | | | | | | | | | | | | | | | 579 |
| | ACC Thr | | | | | | | | | | | | | | | 627 |
| | AUG Met | | | | | | | | | | | | | | | 675 |
| | CUC Leu | | | | | | | | | | | | | | | 723 |
| | UUG Leu | | | | | | | | | | | | | | | 771 |
| | GUG Val 250 | | | | | | | | | | | | | | | 819 |

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| AGC Ser 265 | AUA Ile | GUG Val | AGA Arg | AGA Arg | GCA Ala 270 | GCA Ala | GUA Val | UCA Ser | GCA Ala | GAU Asp 275 | CCA Pro | CUA Leu | GCA Ala | UCU Ser | UUA Leu 280 | 867 |
|-------------------|------------|-------------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------|
| | | AUG Met | | | | | | | | | | | | | | 915 |
| | | AGG Arg | | | | | | | | | | | | | | 963 |
| | | AUG Met 315 | | | | | | | | | | | | | | 1011 |
| | | AAG Lys | | | | | | | | | | | | | | 1059 |
| | | GGC Gly | | | | | | | | | | | | | | 1107 |
| | | UUC Phe | | | | | | | | | | | | | | 1155 |
| | | AGG Arg | | | | | | | | | | | | | | 1203 |
| | | GCU Ala 395 | | | | | | | | | | | | | | 1251 |
| | Met | AUA Ile | Lys | Ala | Val | Arg | Gly | Asp | Leu | Asn | Phe | Val | | | | 1299 |
| | | CGA Arg | | | | | | | | | | | | | | 1347 |
| | | AAA Lys | | | | | | | | | | | | | | 1395 |
| | | GGA Gly | | | | | | | | | | | | | | 1443 |
| | | AUG Met 475 | | | | | | | | | | | | | | 1491 |

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| AGC Ser 490 | | | | | | | | | | | | | 153 | 9 |
|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|------|---|
| GAC Asp | | | | | | | | | | | | | 158 | 7 |
| CAG Gln | | | | | | | | | | | | | 163 | 5 |
| GAG Glu | | | | | | | | | | | | | 168 | 3 |
| AUC Ile | | | | | | | | | | | | | 173 | 1 |
| AUG Met 570 | | | | | | | | | | | | | 177 | 9 |
| AAG Lys | | | | | | | | | | | | | 182 | 7 |
| CAA Gln | | | | | | | | | | | | | 187 | 5 |
| CUU Leu | | | | | | | | | | | | | 192 | 3 |
| UCU Ser | Ser | Leu | Thr | Val | Val | Arg | Gly | Ser | Gly | Met | Arg | | 197 | 1 |
| AGG Arg 650 | | | | | | | | | | | | | 201 | 9 |
| ACA Thr | | | | | | | | | | | | | 206 | 7 |
| GGC Gly | | | | | | | | | | | | | 211 | 5 |
| GGC Gly | | | | | | | | | | | | | 2163 | 3 |

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|------------|-----------|-------------------|------------|-----------|-----------|-----------|-----------------|------------|-----------|-----------|-----------|------------|------------|-----------|-----------|------|
| | | | CUU Leu | | | | | | | | | | | | | 2211 |
| | | | GUG Val | | | | | | | | | | | | | 2259 |
| | | | CÁG G1n | | | | | | | | | | | | | 2304 |
| UAAI | JGUU | SAA (| JAGUI | JUAA | AA AG | CGAC | CUUG | J UU(| CUACI | J | | | | | | 2341 |
| | | | | | | | | | | | | | | | | |
| (2) | INFO | ORMA ⁻ | TION | FOR | SEQ | ID I | NO:10 | 5: | | | | | | | | |
| | (| (i) : | SEQUI | ENCE | CHAI | RACTI | ERIS | TICS | : | | | | | | | |
| | | | (A) |) LEI | NGTH | : 759 | am [.] | ino a | acid: | 5 | | | | | | |
| | | | (B) |) TYI | PE: a | amino | ac. | i d | | | | | | | | |
| | | | (D) |) TOI | POL00 | ay: ' | linea | ar | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| | (i | ii) / | MOLE | CULE | TYPI | E: p | rote | in | | | | | | | | |
| | (> | ci) : | SEQUI | ENCE | DES | CRIP | FION: | : SEC | Q ID | NO: 1 | 16: | | | | | |
| Met 1 | Glu | Arg | Ile | Lys 5 | Glu | Leu | Arg | Asn | Leu 10 | Met | Ser | Gln | Ser | Arg 15 | Thr | |
| Arg | G1u | Ile | Leu 20 | Thr | Lys | Thr | Thr | Va1 25 | Asp | His | Met | Ala | Ile 30 | Ile | Lys | |
| Lys | Tyr | Thr 35 | Ser | Gly | Arg | Gln | G1u 40 | Lys | Asn | Pro | Ser | Leu 45 | Arg | Met | Lys | |
| Trp | Met 50 | Met | Ala | Met | Lys | Tyr 55 | Pro | Ile | Thr | Ala | Asp 60 | Lys | Arg | Ile | Thr | |
| G1 u 65 | Met | Ile | Pro | G1u | Arg 70 | Asn | Glu | G1 n | Gly | G1n 75 | Thr | Leu | Trp | Ser | Lys 80 | |
| Met | Ser | Asp | Ala | G1y 85 | Ser | Asp | Arg | Val | Met 90 | Val | Ser | Pro | Leu | Ala 95 | Val | |
| Thr | Trp | Trp | Asn 100 | Arg | Asn | Gly | Pro | Met 105 | Thr | Ser | Thr | Val | His 110 | Tyr | Pro | |
| Lys | Ile | Tyr 115 | Lys | Thr | Tyr | Phe | Glu 120 | Lys | Val | Glu | Arg | Leu 125 | Lys | His | Gly | |

Thr Phe Gly Pro Val His Phe Arg Asn Gln Val Lys Ile Arg Arg Arg Val Asp Ile Asn Pro Gly His Ala Asp Leu Ser Ala Lys Glu Ala Gln 150 Asp Val Ile Met Glu Val Val Phe Pro Asn Glu Val Gly Ala Arg Ile Leu Thr Ser Glu Ser Gln Leu Thr Ile Thr Lys Glu Lys Lys Glu Glu Leu Gln Asp Cys Lys Ile Ser Pro Leu Met Val Ala Tyr Met Leu Glu 200 Arg Glu Leu Val Arg Lys Thr Arg Phe Leu Pro Val Ala Gly Gly Thr Ser Ser Val Tyr Ile Glu Val Leu His Leu Thr Gln Gly Thr Cys Trp 230 Glu Gln Met Tyr Thr Pro Gly Gly Glu Val Arg Asn Asp Asp Val Asp Gln Ser Leu Ile Ile Ala Ala Arg Ser Ile Val Arg Arg Ala Ala Val 265 270 Ser Ala Asp Pro Leu Ala Ser Leu Leu Glu Met Cys His Ser Thr Gln 280 Ile Gly Gly Thr Arg Met Val Asp Ile Leu Arg Gln Asn Pro Thr Glu 295 300 Glu Gln Ala Val Glu Ile Cys Lys Ala Ala Met Gly Leu Arg Ile Ser 320 305 310 Ser Ser Phe Ser Phe Gly Gly Phe Thr Phe Lys Arg Thr Ser Gly Ser 330 Ser Val Lys Arg Glu Glu Glu Val Leu Thr Gly Asn Leu Gln Thr Leu 345 Lys Ile Arg Val His Glu Gly Tyr Glu Glu Phe Thr Met Val Gly Lys 355 Arg Ala Thr Ala Ile Leu Arg Lys Ala Thr Arg Arg Leu Ile Gln Leu 375 Ile Val Ser Gly Arg Asp Glu Gln Ser Ile Ala Glu Ala Ile Ile Val 390 395 Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly 405 415 410 Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His 425

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Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn 440 Trp Gly Ile Glu His Ile Asp Asn Val Met Gly Met Ile Gly Val Leu Pro Asp Met Thr Pro Ser Thr Glu Met Ser Met Arg Gly Val Arg Val 480 470 Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Ala Glu Arg Val Val 490 Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Val Leu Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr 520 Ile Thr Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser 530 Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Thr Val Lys Ile Gln Trp Ser Gln Asn Pro Thr Met Leu Tyr Asn Lys Met Glu 570 Phe Glu Pro Phe Gln Ser Leu Val Pro Lys Ala Ile Arg Gly Gln Tyr 580 Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly 600 Thr Phe Asp Thr Thr Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala 610 615 620 Pro Pro Lys Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val 625 630 635 Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Ile Phe 650 Asn Tyr Asn Lys Thr Thr Lys Arg Leu Thr Ile Leu Gly Lys Asp Ala 660 670 Gly Thr Leu Thr Glu Asp Pro Asp Glu Gly Thr Ser Gly Val Glu Ser 680 Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asp Arg Arg Tyr 695 Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Asn Leu Ala Lys Gly Glu 705 710 715 720 Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Val Val Leu Val Met Lys

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725

730

735

Arg Lys Arg Asn Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys
740 745 750

Arg Ile Arg Met Ala Ile Asn 755

- (2) INFORMATION FOR SEQ ID NO:17:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1773 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: RNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: cold-adapted "Master Strain" A/Ann Arbor/6/60 7PI (H2N2)
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: HA
 - (ix) FEATURE:
 - (A) NAME/KEY: mutation
 - (B) LOCATION: replace(144, "u")
 - (D) OTHER INFORMATION: /gene= "HA" /note= "u in ca "master" strain; a in w2(3)" /citation= ([1])
 - (ix) FEATURE:
 - (A) NAME/KEY: mutation

- (B) LOCATION: replace(455, "a")
- (D) OTHER INFORMATION: /gene= "HA" /note= "a in ca "master" strain; g in wt2(3)" /citation= ([1])

(ix) FEATURE:

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- (A) NAME/KEY: mutation
- (B) LOCATION: replace(729, "c")

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 44..1729
- (D) OTHER INFORMATION: /product= "hemagglutinin" /gene= "HA" /note= "hemagglutinin protein" /citation= ([1])

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G
- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA
- (G) DATE: 1993
- (K) RELEVANT RESIDUES IN SEQ ID NO:17: FROM 1 TO 1773
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

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| | | | | | | ACA Thr | | | | | | | | | | | 103 |
|-----|-----|-----|-----|-----|-----|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|---|-----|
| | | | | | | UCC Ser | | | | | | | | | | | 151 |
| | | | | | | CAU His | | | | | | | | | | | 199 |
| | | | | | | CUA Leu | | | | | | | | | | | 247 |
| | | | | | | UGG Trp 75 | | | | | | | | | | | 295 |
| | | | | | | UGG Trp | | | | | | | | | | , | 343 |
| | | | | | | CCA Pro | | | | | | | | | | | 391 |
| | | | | | | GUG Val | | - | | | | | | | | | 439 |
| | | | | | | CAG Gln | | | | | | | | | | | 487 |
| | | | | | | CCA Pro 155 | | | | | | | | | | | 535 |
| | | | | | | UAU Tyr | | | | | | | | | | | 583 |
| | | | | | | CUA Leu | | | | | | | | | | | 631 |
| | | | | | | ACA Thr | | | | | | | | | | | 679 |
| UCC | GUA | GGC | ACA | UCA | ACA | UUG | AAC | AAA | AGG | UCA | ACC | CCA | GAA | AUA | GCA | | 727 |

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| Ser | Val | Gly 215 | Thr | Ser | Thr | Leu | Asn 220 | Lys | Arg | Ser | Thr | Pro 225 | Glu | Ile | Ala | |
|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-------------------|-----|------|
| | | | | | | | | | | | | | | UCU Ser | | 775 |
| | | | | | | | | | | | | | | GGU Gly | | 823 |
| | | | _ | - | | | | | | | | | | AGU Ser 275 | | 871 |
| | | | | | | | | | | | | | | AAA Lys | | 919 |
| | | | | | | | | | | | | | | AAU Asn | | 967 |
| | | | | | | | | | | | | | | GAG Glu | | 1015 |
| | | | | | | | | | | | | | | UCA Ser | | 1063 |
| | | | | | | | | | | | | | | CAA G1n 355 | | 1111 |
| | | | | | | | | | | | | | | GGA Gly | | 1159 |
| | | | | | | | | | | | | | | GGA Gly | | 1207 |
| | | | | | | | | | | | | | | UUU Phe | | 1255 |
| | | | | | | | | | | | | | | AAC Asn | | 1303 |
| | | | | | | | | | | | | | | AAU Asn 435 | | 1351 |

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| | CUU Leu | | | | | | | | | | | | | | 1399 |
|-----|-------------------|-------|-------|-------|-------|-------|---------------|-----|-------|------|------|---|--|--|------|
| | AAU Asn | | | | | | | | | | | | | | 1447 |
| | GUC Val 470 | | | | | | | | | | | | | | 1495 |
| | GAU Asp | | | | | | | | | | | | | | 1543 |
| | UAU Tyr | | | | | | | | | | | | | | 1591 |
| | UUG Leu | | | | | | | | | | | | | | 1639 |
| | GCA Ala | | | | | | | | | | | | | | 1687 |
| | AUG Met 550 | | | | | | | | | | | | | | 1729 |
| UGA | JUAUA | AAG (| JCAUL | JUUAL | JA AL | JUAAA | \AAC <i>A</i> | CC(| CUUGU | JUUC | UACI | J | | | 1773 |

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 562 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Met Ala Ile Ile Tyr Leu Ile Leu Leu Phe Thr Ala Val Arg Gly Asp $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

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Lys Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Glu Thr Val Asp 20 Thr Ile Leu Glu Arg Asn Val Thr Val Thr His Ala Lys Asp Ile Leu 40 Glu Lys Thr His Asn Gly Lys Leu Cys Lys Leu Asn Gly Ile Pro Pro Leu Glu Leu Gly Asp Cys Ser Ile Ala Gly Trp Leu Leu Gly Asn Pro Glu Cys Asp Arg Leu Leu Ser Val Pro Glu Trp Ser Tyr Ile Met Glu Lys Glu Asn Pro Arg Asn Gly Leu Cys Tyr Pro Gly Asn Phe Asn Asp Tyr Glu Glu Leu Lys His Leu Leu Ser Ser Val Lys His Phe Glu Lys Val Lys Ile Leu Pro Lys Asp Arg Trp Thr Gln His Thr Thr Gly Gly Ser Gln Ala Cys Ala Val Ser Gly Asn Pro Ser Phe Phe Arg Asn 150 155 160 Met Val Trp Leu Thr Glu Glu Gly Ser Asn Tyr Pro Val Ala Lys Gly 165 Ser Tyr Asn Asn Thr Ser Gly Glu Gln Met Leu Ile Ile Trp Gly Val 185 His His Pro Ile Asp Glu Thr Glu Gln Arg Thr Leu Tyr Gln Asn Val 195 205 Gly Thr Tyr Val Ser Val Gly Thr Ser Thr Leu Asn Lys Arg Ser Thr 215 220 Pro Glu Ile Ala Thr Arg Pro Lys Val Asn Gly Leu Gly Ser Arg Met Glu Phe Ser Trp Thr Leu Leu Asp Met Trp Asp Thr Ile Asn Phe Glu 255 Ser Thr Gly Asn Leu Ile Ala Pro Glu Tyr Gly Phe Lys Ile Ser Lys 260 270 Arg Gly Ser Ser Gly Ile Met Lys Thr Glu Gly Thr Leu Glu Asn Cys 280 Glu Thr Lys Cys Gln Thr Pro Leu Gly Ala Ile Asn Thr Thr Leu Pro 290 300 Phe His Asn Val His Pro Leu Thr Ile Gly Glu Cys Pro Lys Tyr Val

320 305 310 315 Lys Ser Glu Lys Leu Val Leu Ala Thr Gly Leu Arg Asn Val Pro Gln 330 Ile Glu Ser Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe Ile Glu Gly Gly Trp Gln Gly Met Val Asp Gly Trp Tyr Gly Tyr His His Ser Asn Asp Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu Ser Thr Gln Lys Ala 375 Phe Asp Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu Lys Ile Asn Thr Gln Phe Glu Ala Val Gly Lys Glu Phe Ser Asn Leu Glu Arg Arg 410 Leu Glu Asn Leu Asn Lys Lys Met Glu Asp Gly Phe Leu Asp Val Trp 420 425 Thr Tyr Asn Ala Glu Leu Leu Val Leu Met Glu Asn Glu Arg Thr Leu 435 440 Asp Phe His Asp Ser Asn Val Lys Asn Leu Tyr Asp Lys Val Arg Met Gln Leu Arg Asp Asn Val Lys Glu Leu Gly Asn Gly Cys Phe Glu Phe Tyr His Lys Cys Asp Asp Glu Cys Met Asn Ser Val Lys Asn Gly Thr 490 Tyr Asp Tyr Pro Lys Tyr Glu Glu Glu Ser Lys Leu Asn Arg Asn Glu 505 510 Ile Lys Gly Val Lys Leu Ser Ser Met Gly Val Cys Arg Ile Leu Ala 515 520 Ile Tyr Ala Thr Val Ala Gly Ser Leu Ser Leu Ala Ile Met Met Ala 535 540 Gly Ile Ser Phe Trp Met Cys Ser Asn Gly Ser Leu Gln Cys Arg Ile 560 545 555 Cys Ile

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1467 base pairs

```
(B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: RNA (genomic)
 (vi) ORIGINAL SOURCE:
       (A) ORGANISM: Influenza virus
       (B) STRAIN: cold-adapted "Master Strain" A/Ann Arbor/6/60 7PI
                   (H2N2)
(vii) IMMEDIATE SOURCE:
       (B) CLONE: NA
 (ix) FEATURE:
       (A) NAME/KEY: mutation
       (B) LOCATION: replace(394, "u")
       (D) OTHER INFORMATION: /product= "Neuraminidase"
                              /gene= "NA"
                              /note= "u in ca "master" strain; c in
                              wt2(3)"
                              /citation= ([1])
 (ix) FEATURE:
       (A) NAME/KEY: mutation
       (B) LOCATION: replace(604, "u")
       (D) OTHER INFORMATION: /product= "Neuraminidase"
                              /gene= "NA"
                              /note= "u in ca "master" strain; a in
                              wt2(3)"
                              /citation= ([1])
(ix) FEATURE:
       (A) NAME/KEY: CDS
      (B) LOCATION: 20..1426
```

(D) OTHER INFORMATION: /product= "neuraminidase"

/gene= "NA"

/note= "neuraminidase protein"
/citation= ([1])

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|---|---|--|
| M | • | |

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G
- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) Influenza Virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA
- (G) DATE: 1993
- (K) RELEVANT RESIDUES IN SEQ ID NO:19: FROM 1 TO 1467

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

| AGC | AAAA | GCA (| GGAGI | JGAA | | | | | | | J GGC e Gly) | 52 |
|-----|------|-------|-------|------|------|-------------------|------|------|---|------|---------------------|-----|
| | | | | | | ACA Thr | | | | | | 100 |
| | | | | | | UUG Leu 35 | | | | | | 148 |
| | | | | | | AUG Met | | | | | | 196 |
| | | | | | | UAU Tyr | | | | | | 244 |
| | | | | | | GGA Gly | | | | | | 292 |
| | | | _ | | | CCU Pro | | | _ | | - | 340 |
| | | | | | | UGG Trp 115 | | | | | | 388 |

| UGC Cys | GAU Asp 125 | CCU Pro | GGC Gly | AAG Lys | UGU Cys | UAU Tyr 130 | CAA Gln | UUU Phe | GCA Ala | CUC Leu | GGG Gly 135 | CAG Gln | GGG Gly | ACC Thr | ACA Thr | 436 |
|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|-------------------|------------|-------|
| | | | | | | | | | | | | | | CCU Pro | | . 484 |
| | | | | | | | | | | | | | | GGA Gly 170 | | 532 |
| | | | | | | | | | | | | | | GGA Gly | | 580 |
| | | | | | | | | | | | | | | ACU Thr | | 628 |
| | | | | | | | | | | | | | | UGG Trp | | 676 |
| | | | | | | | | | | | | | | AAU Asn | | 724 |
| | | | | | | | | | | | | | | GCU Ala 250 | | 772 |
| | | | | | | | | | | | | | | GGC Gly | | 820 |
| | | | | | | | | | | | | | | CCU Pro | | 868 |
| | | | | | | | | | | | | | | UCU Ser | | 916 |
| | | | | | | | | | | | | | | UCC Ser | | 964 |
| | | | | | | | | | | | | | | GAC Asp 330 | | 1012 |
| | | | | | | | | | | | | | | AAU Asn | | 1060 |

 $\mathfrak{g}_{\mathfrak{l}}$

| | | | | | | | GGA Gly | | | | | | | 110 | 80 |
|-----|------|-------|-------|-------|-------------------|--|------------------------|------|------|-------|------|-------|----|-----|----|
| | | | | | | | GGU Gly | | | | | | | 11 | 56 |
| | | | | | | | AAA Lys | | | | | | | 120 | 04 |
| _ | - | | | _ | | | GGU G1 y 405 | _ | | | | | | 12 | 52 |
| | | | | | | | UGC Cys | | | | | | | 130 | 00 |
| | | | | | | | UGG Trp | | | | | | | 13 | 48 |
| | | | | | | | UAU Tyr | | | | | | | 13 | 96 |
| | | | | | AAU Asn 465 | | AUA Ile | UAA(| CGUU | JCG (| CAAU | JUUA(| SA | 14 | 46 |
| AAA | AACU | JCC (| JUGUL | JUCUA | AC U | | | | | | | | | 14 | 67 |

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 469 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Met Asn Pro Asn Gln Lys Thr Ile Thr Ile Gly Ser Val Ser Leu Thr 1 5 10 15

al

Ile Ala Thr Val Cys Phe Leu Met Gln Ile Ala Ile Leu Ala Thr Thr Val Thr Leu His Leu Lys Gln His Glu Cys Asp Ser Pro Ala Ser Asn Gln Val Met Pro Cys Glu Pro Ile Ile Ile Glu Arg Asn Ile Thr Glu Ile Val Tyr Leu Asn Asn Thr Thr Ile Glu Lys Glu Ile Cys Pro Glu Val Val Gly Tyr Arg Asn Trp Ser Lys Pro Gln Cys Gln Ile Thr Gly Phe Ala Pro Phe Ser Lys Asp Asn Ser Ile Arg Leu Ser Ala Gly Gly Asp Ile Trp Val Thr Arg Glu Pro Tyr Val Ser Cys Asp Pro Gly Lys Cys Tyr Gln Phe Ala Leu Gly Gln Gly Thr Thr Leu Asp Asn Lys His Ser Asn Gly Thr Ile His Asp Arg Ile Pro His Arg Thr Leu Leu Met 160 Asn Glu Leu Gly Val Pro Phe His Leu Gly Thr Lys Gln Val Cys Ala Ala Trp Ser Ser Ser Cys His Asp Gly Lys Ala Trp Leu His Val Cys Val Thr Gly Asp Asp Arg Asn Ala Thr Ala Ser Phe Ile Tyr Asp 195 Gly Lys Leu Val Asp Ser Ile Gly Ser Trp. Ser Gln Asn Val Leu Arg 215 Thr Gln Glu Ser Glu Cys Val Cys Ile Asn Gly Thr Cys Thr Val Val Met Thr Asp Gly Ser Ala Ser Gly Arg Ala Asp Thr Arg Ile Leu Phe 255 Ile Lys Glu Gly Lys Ile Val His Ile Gly Pro Leu Ser Gly Ser Ala 265 Gln His Val Glu Glu Cys Ser Cys Tyr Pro Arg Tyr Pro Asp Val Arg Cys Ile Cys Arg Asp Asn Trp Lys Gly Ser Asn Arg Pro Val Ile Asp 290 Ile Asn Met Glu Asp Tyr Ser Ile Asp Ser Ser Tyr Val Cys Ser Gly

320 305 310 315 Leu Val Gly Asp Thr Pro Arg Asn Asp Asp Ser Ser Asn Ser Asn 325 330 335 Cys Arg Asp Pro Asn Asn Glu Arg Gly Asn Pro Gly Val Lys Gly Trp Ala Phe Asp Asn Gly Asp Asp Val Trp Met Gly Arg Thr Ile Ser Lys 360 Asp Leu Arg Ser Gly Tyr Glu Thr Phe Lys Val Ile Gly Gly Trp Ser 380 Thr Pro Asn Ser Lys Ser Gln Val Asn Arg Gln Val Ile Val Asp Asn Asn Asn Trp Ser Gly Tyr Ser Gly Ile Phe Ser Val Glu Gly Lys Ser Cys Ile Asn Arg Cys Phe Tyr Val Glu Leu Ile Arg Gly Arg Pro Gln 420 425 430 Glu Thr Arg Val Trp Trp Thr Ser Asn Ser Ile Val Val Phe Cys Gly 435 440 Thr Ser Gly Thr Tyr Gly Thr Gly Ser Trp Pro Asp Gly Ala Asn Ile 460 Asn Phe Met Pro Ile

(2) INFORMATION FOR SEQ ID NO:21:

465

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 890 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: wild type A/Ann Arbor/6/60 (H2N2) Egg Passage 2(3)

11

(vii) IMMEDIATE SOURCE:

(B) CLONE: NS

(ix) FEATURE:

- (A) NAME/KEY: exon
- (B) LOCATION: 27..56
- (D) OTHER INFORMATION: /product= "nonstructural protein NS2" /gene= "NS" /note= "nonstructural protein NS2" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(483, "a")
- (D) OTHER INFORMATION: /note= "a in ca "master" strain and in wt2(3); g in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: exon
- (B) LOCATION: 529..861
- (D) OTHER INFORMATION: /product= "nonstructural protein NS2" /gene= "NS" /note= "nonstructural protein NS2" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(813, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: join(27..56, 529..861)

(D) OTHER INFORMATION: /product= "nonstructural protein NS2" /gene= "NS" /note= "nonstructural protein NS2" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 27..677
- (D) OTHER INFORMATION: /product= "nonstructural protein NS1" /gene= "NS" /note= "nonstructural protein NS1" /citation= ([1][2])

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G
- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA
- (G) DATE: 1993,
- (K) RELEVANT RESIDUES IN SEQ ID NO:21: FROM 1 TO 890

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Cox, N J
 Kitame, F
 Kendal, A P
 Maassab, H F
 Naeve, C
- (B) TITLE: Identification of sequence changes in the cold-adapted live attenuated influenza vaccine strain, A/Ann Arbor/6/60(H2N2)
- (C) JOURNAL: Virology
- (D) VOLUME: 167
- (F) PAGES: 554-567
- (G) DATE: 1988

(K) RELEVANT RESIDUES IN SEQ ID NO:21: FROM 1 TO 890

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

| AGCAAAAGCA GGGUGACAAA GACAUA AUG GAU CCU AAC ACU GUG UCA AGC UUU Met Asp Pro Asn Thr Val Ser Ser Phe 1 5 | | | | | | | | | | | | 53 | | |
|--|--|--|-------------------|--|--|--|--|--|--|--|--|----|--|-----|
| | | | UGC Cys | | | | | | | | | | | 101 |
| | | | GAU Asp | | | | | | | | | | | 149 |
| | | | GGA Gly 45 | | | | | | | | | | | 197 |
| | | | GGA Gly | | | | | | | | | | | 245 |
| | | | CUU Leu | | | | | | | | | | | 293 |
| | | | AUG Met | | | | | | | | | | | 341 |
| | | | CAG Gln | | | | | | | | | | | 389 |
| | | | GAU Asp 125 | | | | | | | | | | | 437 |
| | | | CUA Leu | | | | | | | | | | | 485 |
| | | | GUU Val | | | | | | | | | | | 533 |
| | | | GAU Asp | | | | | | | | | | | 581 |
| | | | GAU Asp | | | | | | | | | | | 629 |

a

| | | | | 190 | | | | | 195 | | | | | 200 | | | |
|-----------|-----------|------------|-------------------|-----------|-----------|------------|-----------|------------|-----------|------------|-----------|-------------------|------------|-----------|-----------|-----------|-----|
| | | | AGC Ser 205 | | | | | | | | | | | | | | 677 |
| UAGA | AAACG | GA . | AAAU | GCGA | AG A | ACAAU | JUAG | G UCA | AAAA | SUUC | GAAG | JAAA | JAA (| SAUG | GCUGA | NU | 737 |
| UGA | AGAAG | GUG . | AGACA | ACAAA | AU UC | SAAGA | AUAAO | C AG | AGAAL | JAGU | UUUG | SAGC/ | AAA I | JAAC | AUUUA | NU | 797 |
| GCA | AGCCL | JUA | CAGC | JGCUA | AU UI | JGAAG | SUGGA | A AC | AAGAG | AUA | AGA | CUUL | JCU (| CGUU | JCAGO | U | 857 |
| UAUl | JUAAL | JGA 1 | UAAA | AAACA | AC CO | CUUGI | JUUCI | J ACI | J | | | | | | | | 890 |
| (2) | INFO |)RMA | TION | FOR | SEQ | ID N | 10:22 | 2: | | | | | | | | | |
| | (| (i) | SEQUE | ENCE | CHAI | RACTE | ERIST | rics: | : | | | | | | | | |
| | | | (A) |) LEI | NGTH | : 217 | 7 am | ino a | acids | 5 | | | | | | | |
| | | | (B) | TYI | PE: a | ami no | o aci | i d | | | | | | | | | |
| | | | (D) |) TO | POLO | 3Y: 1 | linea | ar | | | | | | | | | |
| | (- | :41 | MOLE | ^III E | TVDI | F. n. | cot o | in | | | | | | | | | |
| | (| 11) | MOLE | JULE | 117 | e: pi | ore | 111 | | , * | | | | | | | |
| | () | ci) | SEQUI | ENCE | DES | CRIP | TION: | : SE | Q ID | NO:2 | 22: | | | | | | |
| Met 1 | Asp | Pro | Asn | Thr 5 | Val | Ser | Ser | Phe | Gln 10 | Val | Asp | Cys | Phe | Leu 15 | Trp | | |
| His | Val | Arg | Lys 20 | G1 n | Val | Ala | Asp | G1n 25 | G1 u | Leu | Gly | Asp | A1a 30 | Pro | Phe | | |
| Leu | Asp | Arg 35 | Leu | Arg | Arg | Asp | G1n 40 | Lys | Ser | Leu | Arg | G1 <i>y</i> 45 | Arg | Gly | Ser | | |
| Thr | Leu 50 | Gly | Leu | Asn | Ile | G1 u 55 | Thr | Ala | Thr | Arg | Va1 60 | G1y | Lys | Gln | Ile | | |
| Val 65 | G1u | Arg | Ile | Leu | Lys 70 | G1 u | G1 u | Ser | Asp | G1 u 75 | Ala | Leu | Lys | Met | Thr 80 | | |
| Met | Ala | Ser | Ala | Pro 85 | Ala | Ser | Arg | Tyr | Leu 90 | Thr | Asp | Met | Thr | Ile 95 | G1 u | | |
| G1u | Met | Ser | Arg 100 | Asp | Trp | Phe | Met | Leu 105 | Met | Pro | Lys | Gln | Lys 110 | Val | Ala | | |
| Gly | Pro | Leu 115 | Cys | Ile | Arg | Met | Asp | Gln | Ala | Ile | Met | Asp | Lys | Asn | Ile | | |

| | Ile | Leu 130 | Lys | Ala | Asn | Phe | Ser 135 | Val | Ile | Phe | Asp | Arg 140 | Leu | Glu | Thr | Leu | | |
|---|------------|------------|-------------------|------------|---------------|------------|------------|------------|------------|---------------|------------|------------|------------|------------|------------|----------------|----|-----|
| | 11e 145 | Leu | Leu | Arg | Ala | Phe 150 | Thr | Glu | Thr | Gly | Ala 155 | Ile | Val | Gly | G1u | Ile 160 | | |
| • | Ser | Pro | Leu | Pro | Ser 165 | Leu | Pro | Gly | His | Thr 170 | Asn | G1 u | Asp | Val | Lys 175 | Asn | | |
| 1 | Ala | Ile | Gly | Val 180 | Leu | Пe | Gly | Gly | Leu 185 | Glu | Trp | Asn | Asp | Asn 190 | Thr | Val | | |
| 1 | Arg | Val | Ser 195 | Lys | Thr | Leu | Gln | Arg 200 | Phe | Ala | Trp | Arg | Ser 205 | Ser | Asp | Glu | | |
| , | Asn | Gly 210 | Arg | Pro | Pro | Leu | Thr 215 | Pro | Lys | | | | | | | | | |
| | (2) | INF | ORMA [*] | TION | FOR | SEQ | ID 1 | NO:2 | 3: | | | | | | | | | |
| | | (i) |) SE | QUEN | CE CI | HARA | CTER | ISTI | CS: | | | | | | | | | |
| | | | (/ | A) LI | ENGTI | H: 4 | 18 ba | ase | pair | s | | | | | | | | |
| | | | (1 | B) T' | YPE: | nuc | leic | acio | d | | | | | | | | | |
| | | | • | • | TRANI | | | | | | | | | | | | | |
| | | | - | - | OPOLO | | | | | | | | | | | | | |
| | | (ii) |) MOI | LECU | LE T | YPE: | RNA | (gei | nomi | c) | | | | | | | | |
| | | (ix |) FE/ | ATUR | E: | | | | | | | | | | | | | |
| | | | (/ | A) N | AME/I | KEY: | CDS | | | | | | | | | | | |
| | • | | | | OCAT: THER | | | | | roduc ene= | | | stru | ctura | al pi | rotein | 2" | |
| | | (xi) |) SE(| QUEN | CE DI | ESCR: | IPTI(| ON: S | SEQ : | ID NO | 0:23 | · | | | | | | |
| , | AGC | \AAA(| GCA (| GGGU(| GACA | AA GA | ACAUA | | | | | | | | | C UUU r Phe | | 53 |
| | | | | | AUG Met | | | | | | | | | | | | | 101 |
| (| GAG | GAC | UUG | AAU | GGA | AUG | AUA | ACA | CAG | UUC | GAG | UCU | CUA | AAA | CUC | UAC | | 149 |

| Glu | Asp | Leu | Asn | G1y 30 | Met | Ile | Thr | Gln | Phe 35 | G1u | Ser | Leu | Lys | Leu 40 | Tyr | |
|------|-------|-------|------------------|-----------|-------|-------|------|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|
| | | | CUU Leu 45 | | | | | | | | | | | | | 197 |
| | | | AGA Arg | | | | | | | | | | | | | 245 |
| | | | AGA Arg | | | | | | | | | | | | | 293 |
| | | | AGU Ser | | | | | | | | | | | | | 341 |
| | | | GUG Val | | | | | | | | | | | | | 389 |
| UAAl | JGAUA | AAA A | AAACA | ACCCI | JU GI | JUUCI | JACU | | | | | | | | | 418 |

(2) INFORMATION FOR SEQ ID NO:24:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 121 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Met Asp Pro Asn Thr Val Ser Ser Phe Gln Asp Ile Leu Met Arg Met 1 5 10 15

Ser Lys Met Gln Leu Gly Ser Ser Glu Asp Leu Asn Gly Met Ile 20 25 30

Thr Gln Phe Glu Ser Leu Lys Leu Tyr Arg Asp Ser Leu Gly Glu Ala

Val Met Arg Met Gly Asp Leu His Ser Leu Gln Asn Arg Asn Gly Lys 50 55 60

Trp Arg Glu Gln Leu Gly Gln Lys Phe Glu Glu Ile Arg Trp Leu Ile

W

65 70 75 80

Glu Glu Val Arg His Lys Leu Lys Ile Thr Glu Asn Ser Phe Glu Gln 85 90 95

Ile Thr Phe Met Gln Ala Leu Gln Leu Leu Phe Glu Val Glu Gln Glu 100 105 110

Ile Arg Thr Phe Ser Phe Gln Leu Ile 115 120

- (2) INFORMATION FOR SEQ ID NO:25:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1027 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: RNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: wild type A/Ann Arbor/6/60 (H2N2) Egg Passage 2(3)
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: M
 - (ix) FEATURE:
 - (A) NAME/KEY: exon
 - (B) LOCATION: 26..51
 - (D) OTHER INFORMATION: /product= "matrix protein M2" /gene= "M" /note= "matrix protein M2" /citation= ([1][2])
 - (ix) FEATURE:
 - (A) NAME/KEY: exon

al

(B) LOCATION: 740..1004

(D) OTHER INFORMATION: /product= "matrix protein M2" /gene= "M" /note= "matrix protein M2" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(969, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3); g in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: join(26..51, 740..1004)
- (D) OTHER INFORMATION: /product= "matrix protein M2" /gene= "M" /note= "matrix protein M2" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 26..781
- (D) OTHER INFORMATION: /product= "matrix protein M1" /gene= "M" /note= "matrix protein M1" /citation= ([1][2])

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G
- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA

| | | ((| 3) D/ | ATE: | 1993 | 3 | | | | | | | | | | |
|-----|------|-------|-------|-------|-------|----------------|-------------------------------|------------------------|-------|----------------|---------------|---------------|---------------|------------------|-------|-----------------------|
| | | (1 | () RE | ELEVA | ANT F | RESI | OUES | IN S | SEQ 1 | D NO | 25: | : FR(|)M 1 | TO 1 | 1027 | |
| | (x) | PUE | BLICA | ATION | INI | FORMA | ATION | ۱: | | | | | | | | |
| | | (/ | A) Al | JTHOI | 1 | (itar (enda | ne, F al, <i>F</i> sab, | A P | | | | | | | | |
| | | (8 | 3) T | [TLE: | liv | ve at | tteni | tion uated (H2N2 | d in | seque fluer | ence nza v | chai vacci | nges ine s | in 1 strai | the d | cold-adapted A/Ann |
| | | ((| C) J(| DURN/ | AL: \ | /iro | logy | | | | | | | | | |
| | | (1 |) V(| DLUMI | E: 16 | 57 | | | | | | | | | | |
| | | (1 | F) P/ | AGES | : 554 | 1-557 | 7 | | | | | | | | | |
| | | ((| G) D/ | ATE: | 1988 | 3 | | | | | | | | | • | |
| | | • | • | | | | DUES | IN S | SEO 1 | ED NO | 0:25 | : FR(| OM 1 | TO : | 1027 | |
| | | | , | | | | | | | | | | | | | |
| | (xi) | SE | QUENC | CE DI | ESCR: | [PTI | ON: S | SEQ : | ID NO |):25 | : | | | | | |
| AGC | AAA(| GCA (| GGUA | GAUAI | JU G/ | AAAG | | | | | | | | GAA Glu | | 52 |
| | | | | | | | | | | | | | | AUC Ile | | 100 |
| | | | | | | | | | | | | | | GAG Glu 40 | | 148 |
| | | | | | | | | | | | | | | ACU Thr | | 196 |
| | | | | | | | | | | | | | | CGA Arg | | 244 |
| | | | | | | | | | | | | | | GGG Gly | | 292 |

CCA AAU AAC AUG GAC AGA GCA GUU AAA CUG UAU AGA AAG CUU AAG AGG 340

Pro Asn Asn Met Asp Arg Ala Val Lys Leu Tyr Arg Lys Leu Lys Arg 95 100 105 GAG AUA ACA UUC CAU GGG GCC AAA GAA AUA GCG CUC AGU UAU UCU GCU 388 Glu Ile Thr Phe His Gly Ala Lys Glu Ile Ala Leu Ser Tyr Ser Ala 110 115 120 GGU GCA CUU GCC AGU UGU AUG GGC CUC AUA UAC AAC AGG AUG GGG GCU 436 Gly Ala Leu Ala Ser Cys Met Gly Leu Ile Tyr Asn Arg Met Gly Ala 130 GUG ACC ACU GAA GUG GUC UUA GGC CUG GUA UGU GCA ACC UGU GAA CAG 484 Val Thr Thr Glu Val Val Leu Gly Leu Val Cys Ala Thr Cys Glu Gln 140 145 AUU GCU GAC UCC CAG CAU AGG UCU CAU AGG CAA AUG GUG ACA ACA ACC 532 Ile Ala Asp Ser Gln His Arg Ser His Arg Gln Met Val Thr Thr 160 165 AAU CCA CUA AUA AGA CAU GAG AAC AGA AUG GUU CUG GCC AGC ACU ACA 580 Asn Pro Leu Ile Arg His Glu Asn Arg Met Val Leu Ala Ser Thr Thr 170 175 180 185 GCU AAG GCU AUG GAG CAA AUG GCU GGA UCG AGU GAG CAA GCA GCA GAG 628 Ala Lys Ala Met Glu Gln Met Ala Gly Ser Ser Glu Gln Ala Ala Glu 190 195 200 GCC AUG GAG GUU GCU AGU CAG GCC AGG CAA AUG GUG CAG GCA AUG AGA 676 Ala Met Glu Val Ala Ser Gln Ala Arg Gln Met Val Gln Ala Met Arg 205 210 GUU AUU GGG ACU CAU CCU AGC UCC AGU GCU GGU CUA AAA AAU GAU CUU 724 Val Ile Gly Thr His Pro Ser Ser Ser Ala Gly Leu Lys Asn Asp Leu 225 CUU GAA AAU UUG CAG GCC UAU CAG AAA CGA AUG GGG GUG CAG AUG CAA 772 Leu Glu Asn Leu Gln Ala Tyr Gln Lys Arg Met Gly Val Gln Met Gln 235 240 245 CGA UUC AAG UGACCCUCUU GUUGUUGCCG CGAGUAUCAU UGGGAUCUUG 821 Arg Phe Lys 250 CACUUGAUAU UGUGGAUUCU UGAUCAUCUU UUUUUCAAAU GCAUUUAUCG CUUCUUUAAA 881 CACGGUCUGA AAAGAGGGCC UUCUACGGAA GGAGUACCAG AGUCUAUGAG GGAAGAAUAU 941 CGAAAGGAAC AGCAGAGUGC UGUGGAUUCU GACGAUAGUC AUUUUGUCAG CAUAGAGCUG 1001 1027 GAGUAAAAA CUACCUUGUU UCUACU

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 252 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Ile Pro 1 5 10 15

Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe 20 25 30

Ala Gly Lys Asn Thr Asp Leu Glu Ala Leu Met Glu Trp Leu Lys Thr 35 40 45

Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe 50 55 60

Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val
65 70 75 80

Gln Asn Ala Leu Asn Gly Asn Gly Asp Pro Asn Asn Met Asp Arg Ala 85 90 95

Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala 100 105 110

Lys Glu Ile Ala Leu Ser Tyr Ser Ala Gly Ala Leu Ala Ser Cys Met 115 120 125

Gly Leu Ile Tyr Asn Arg Met Gly Ala Val Thr Thr Glu Val Val Leu 130 135 140

Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg 145 150 155 160

Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu 165 170 175

Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met 180 185 190

Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Gln 195 200 205

Ala Arg Gln Met Val Gln Ala Met Arg Val Ile Gly Thr His Pro Ser 210 215 220

| Ser Ser Ala Gly Leu Lys Asn Asp Leu Leu Glu Asn Leu Gln Ala Tyr 225 230 235 240 | |
|--|-----|
| Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys 245 250 | |
| (2) INFORMATION FOR SEQ ID NO:27: | |
| (i) SEQUENCE CHARACTERISTICS: | |
| (A) LENGTH: 339 base pairs | |
| (B) TYPE: nucleic acid | |
| (C) STRANDEDNESS: single | |
| (D) TOPOLOGY: linear | |
| (ii) MOLECULE TYPE: RNA (genomic) | |
| (ix) FEATURE: | |
| (A) NAME/KEY: CDS | |
| (B) LOCATION: 26316 | |
| (D) OTHER INFORMATION: /product= "Matrix M2" | |
| | |
| (xi) SEQUENCE DESCRIPTION: SEQ ID NO:27: | |
| AGCAAAAGCA GGUAGAUAUU GAAAG AUG AGU CUU CUA ACC GAG GUC GAA ACG Met Ser Leu Leu Thr Glu Val Glu Thr 1 5 | 52 |
| CCU AUC AGA AAC GAA UGG GGG UGC AGA UGC AAC GAU UCA AGU GAC CCU Pro Ile Arg Asn Glu Trp Gly Cys Arg Cys Asn Asp Ser Ser Asp Pro 10 25 | 100 |
| CUU GUU GUU GCC GCG AGU AUC AUU GGG AUC UUG CAC UUG AUA UUG UGG Leu Val Val Ala Ala Ser Ile Ile Gly Ile Leu His Leu Ile Leu Trp 30 35 40 | 148 |
| AUU CUU GAU CAU CUU UUU UUC AAA UGC AUU UAU CGC UUC UUU AAA CAC Ile Leu Asp His Leu Phe Phe Lys Cys Ile Tyr Arg Phe Phe Lys His 45 50 55 | 196 |
| GGU CUG AAA AGA GGG CCU UCU ACG GAA GGA GUA CCA GAG UCU AUG AGG Gly Leu Lys Arg Gly Pro Ser Thr Glu Gly Val Pro Glu Ser Met Arg 60 65 70 | 244 |

W

GAA GAA UAU CGA AAG GAA CAG CAG AGU GCU GUG GAU UCU GAC GAU AGU Glu Glu Tyr Arg Lys Glu Gln Gln Ser Ala Val Asp Ser Asp Asp Ser 75 80 85 292

CAU UUU GUC AGC AUA GAG CUG GAG UAAAAAACUA CCUUGUUUCU ACU His Phe Val Ser Ile Glu Leu Glu 90 95

339

(2) INFORMATION FOR SEQ ID NO:28:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 97 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp Pro Leu Val Val Ala Ala Ser Ile 20 25 30

Ile Gly Ile Leu His Leu Ile Leu Trp Ile Leu Asp His Leu Phe Phe 35 40 45

Lys Cys Ile Tyr Arg Phe Phe Lys His Gly Leu Lys Arg Gly Pro Ser 50 55 60

Thr Glu Gly Val Pro Glu Ser Met Arg Glu Glu Tyr Arg Lys Glu Gln
65 70 75 80

Gln Ser Ala Val Asp Ser Asp Asp Ser His Phe Val Ser Ile Glu Leu 85 90 95

Glu

- (2) INFORMATION FOR SEQ ID NO:29:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2341 base pairs
 - (B) TYPE: nucleic acid

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: wild type A/Ann Arbor/6/60 (H2N2) egg passage 2(3)
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: PB2
- (ix) FEATURE:
 - (A) NAME/KEY: mutation
 - (B) LOCATION: replace(141, "a")
 - (D) OTHER INFORMATION: /note= "g in ca "master" strain; a in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])
- (ix) FEATURE:
 - (A) NAME/KEY: conflict
 - (B) LOCATION: replace(426, "c")
 - (D) OTHER INFORMATION: /note= "c in ca "master" strain and in wt2(3); u in 1988 reported wild type E28-32 strain" /citation= ([1][2])
- (ix) FEATURE:
 - (A) NAME/KEY: conflict
 - (B) LOCATION: replace(714, "u")
 - (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3); c in 1988 reported wild type E28-32 strain" /citation= ([1][2])

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(821, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace (963, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1182, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1212, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3); c in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1353, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in

wt2(3); u in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1923, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: mutation
- (B) LOCATION: replace(1933, "u")
- (D) OTHER INFORMATION: /note= "c in ca "master" strain; u in wt2(3); u in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 28..2304
- (D) OTHER INFORMATION: /product= "polymerase basic 2" /gene= "PB2" /note= "polymerase basic 2" /citation= ([1][2])

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G
- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA
- (G) DATE: 1993

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(K) RELEVANT RESIDUES IN SEQ ID NO:29: FROM 1 TO 2341

| | (x) |) PUI | BLICA | ATIO | N INI | FORM | ATIO | N: | | | | | | | | |
|-----|-------|-------|-------|----------------------|-------|--|------------------------|------|------------------|-------|------|------|------|------|------|-----------------------|
| | | (/ | A) Al | JTHO | | Cox, Kitar Kenda Maass Naeve | ne, l al, a sab, | A P | | | | | | | | |
| | | (1 | 3) T | [TLE: | liv | | tten | uate | d in | | | | | | | cold-adapted A/Ann |
| | | ((| C) J(| OURNA | AL: 1 | /iro | logy | | | | | | | | | |
| | | (1 |) V(| DLUMI | E: 10 | 57 | | | | | | | | | | |
| | | (1 | F) P/ | AGES | : 554 | 4-567 | 7 | | | | | | | | | • |
| | | ((| G) D/ | ATE: | 1988 | 3 | | | | | | | ٠ | | | |
| | | (1 | K) R | ELEVA | ANT I | RESI | DUES | IN : | SEQ : | ID NO |):29 | : FR | OM 1 | TO 2 | 2341 | |
| | (xi) |) SE(| QUENC | CE DI | ESCR: | [PTI(| ON: S | SEQ | ID NO |):29 | : | | | | | |
| AGC | SAAA(| GCA (| GGUC/ | A UU <i>A</i> | N UA | JUCA | | | AA AG lu Ai | | | | | | | 51 |
| | | | | | | | | | GAG Glu | | | | | | | 99 |
| | | | | | | | | | UAC Tyr | | | | | | | 147 |
| | | | | | | | | | AUG Met 50 | | | | | | | 195 |

AUU ACA GCC GAC AAG AGG AUA ACA GAA AUG AUU CCU GAG AGA AAU GAG

Ile Thr Ala Asp Lys Arg Ile Thr Glu Met Ile Pro Glu Arg Asn Glu

CAA GGG CAA ACU CUA UGG AGU AAA AUG AGU GAU GCC GGA UCG GAU CGU

Gln Gly Gln Thr Leu Trp Ser Lys Met Ser Asp Ala Gly Ser Asp Arg 80

GUG AUG GUA UCA CCU CUG GCU GUG ACA UGG UGG AAU AGA AAU GGA CCA

Val Met Val Ser Pro Leu Ala Val Thr Trp Trp Asn Arg Asn Gly Pro

65

243

291

339

70

60

75

AUG ACA AGU ACG GUU CAU UAU CCA AAA AUC UAC AAA ACU UAU UUU GAG Met Thr Ser Thr Val His Tyr Pro Lys Ile Tyr Lys Thr Tyr Phe Glu AAA GUC GAA AGG UUA AAA CAU GGA ACC UUU GGC CCU GUC CAU UUU AGA Lys Val Glu Arg Leu Lys His Gly Thr Phe Gly Pro Val His Phe Arg AAC CAA GUC AAA AUA CGC CGA AGA GUU GAC AUA AAU CCU GGU CAU GCA Asn Gln Val Lys Ile Arg Arg Arg Val Asp Ile Asn Pro Gly His Ala GAC CUC AGU GCC AAG GAG GCA CAG GAU GUA AUC AUG GAA GUU GUU UUC Asp Leu Ser Ala Lys Glu Ala Gln Asp Val Ile Met Glu Val Val Phe CCU AAC GAA GUG GGG GCC AGG AUA CUA ACG UCG GAA UCG CAA UUA ACA Pro Asn Glu Val Gly Ala Arg Ile Leu Thr Ser Glu Ser Gln Leu Thr AUA ACC AAA GAG AAA AAA GAA GAA CUC CAG GAU UGC AAA AUU UCA CCU Ile Thr Lys Glu Lys Lys Glu Glu Leu Gln Asp Cys Lys Ile Ser Pro UUG AUG GUU GCG UAC AUG UUA GAG AGA GAA CUU GUC CGA AAA ACG AGA Leu Met Val Ala Tyr Met Leu Glu Arg Glu Leu Val Arg Lys Thr Arg UUU CUC CCA GUU GCU GGU GGA ACA AGC AGU GUG UAC AUU GAA GUG UUG Phe Leu Pro Val Ala Gly Gly Thr Ser Ser Val Tyr Ile Glu Val Leu CAC UUG ACU CAA GGA ACA UGC UGG GAA CAG AUG UAC ACU CCA GGU GGA His Leu Thr Gln Gly Thr Cys Trp Glu Gln Met Tyr Thr Pro Gly Gly GAA GUG AGG AAU GAU GAU GUU GAU CAA AGU CUA AUU AUU GCA GCC AGG Glu Val Arg Asn Asp Asp Val Asp Gln Ser Leu Ile Ile Ala Ala Arg AGC AUA GUG AGA AGA GCA GCA GUA UCA GCA GAU CCA CUA GCA UCU UUA . 867 Ser Ile Val Arg Arg Ala Ala Val Ser Ala Asp Pro Leu Ala Ser Leu UUG GAG AUG UGC CAC AGC ACA CAG AUU GGC GGG ACA AGG AUG GUG GAC Leu Glu Met Cys His Ser Thr Gln Ile Gly Gly Thr Arg Met Val Asp AUU CUU AGG CAG AAC CCA ACA GAA GAG CAA GCU GUG GAA AUA UGC AAG Ile Leu Arg Gln Asn Pro Thr Glu Glu Gln Ala Val Glu Ile Cys Lys GCU GCA AUG GGA CUG AGG AUC AGC UCA UCC UUC AGU UUU GGC GGG UUC

| Ala | Ala | Met 315 | Gly | Leu | Arg | Ile | Ser 320 | Ser | Ser | Phe | Ser | Phe 325 | Gly | Gly | Phe | |
|-----|-----|------------|-----|-----|-----|-----|-------------------|-----|-----|-----|-----|------------|-----|-----|-----|------|
| | | | | | | | UCA Ser | | | | | | | | | 1059 |
| | | | | | | | UUG Leu | | | | | | | | | 1107 |
| | | | | | | | AAA Lys | | | | | | | | | 1155 |
| | | | | | | | CUG Leu | | | | | | | | | 1203 |
| | | | | | | | GUG Val 400 | | | | | | | | | 1251 |
| | | | | | | | GGU Gly | | | | | | | | | 1299 |
| | | | | | | | CAU His | | | | | | | | | 1347 |
| | | | | | | | AAU Asn | | | | | | | | | 1395 |
| | | | | | | | UUA Leu | | | | | | | | | 1443 |
| | Ser | | | | | | GUC Val 480 | | | | | | | | | 1491 |
| | | | | | | | GUG Val | | | | | | | | | 1539 |
| | | | | | | | CUA Leu | | | | | | | | | 1587 |
| | | | | | | | ACA Thr | | | | | | | | | 1635 |
| | | | | | | | | | | | | | | | | |

| | | | | UUG Leu | | | | 1683 |
|--|--|--|--|-------------------|--|--|--|------|
| | | | | AUU I]le | | | | 1731 |
| | | | | GAG G1u | | | | 1779 |
| | | | | GGG Gly | | | | 1827 |
| | | | | UUU Phe 610 | | | | 1875 |
| | | | | CCA Pro | | | | 1923 |
| | | | | GGA Gly | | | | 1971 |
| | | | | UAC Tyr | | | | 2019 |
| | | | | ACU Thr | | | | 2067 |
| | | | | GUU Va1 690 | | | | 2115 |
| | | | | CCA Pro | | | | 2163 |
| | | | | GCU Ala | | | | 2211 |
| | | | | AAA Lys | | | | 2259 |
| | | | | AUU Ile | | | | 2304 |

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(2) INFORMATION FOR SEQ ID NO:30:

a

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 759 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Met Glu Arg Ile Lys Glu Leu Arg Asn Leu Met Ser Gln Ser Arg Thr 1 5 10 15

Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys
20 25 30

Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ser Leu Arg Met Lys
35 40 45

Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Thr 50 55 60

Glu Met Ile Pro Glu Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys
65 70 75 80

Met Ser Asp Ala Gly Ser Asp Arg Val Met Val Ser Pro Leu Ala Val 85 90 95

Thr Trp Trp Asn Arg Asn Gly Pro Met Thr Ser Thr Val His Tyr Pro
100 105 110

Lys Ile Tyr Lys Thr Tyr Phe Glu Lys Val Glu Arg Leu Lys His Gly
115 120 125

Thr Phe Gly Pro Val His Phe Arg Asn Gln Val Lys Ile Arg Arg Arg 130 135 140

Val Asp Ile Asn Pro Gly His Ala Asp Leu Ser Ala Lys Glu Ala Gln 145 150 155 160

Asp Val Ile Met Glu Val Val Phe Pro Asn Glu Val Gly Ala Arg Ile 165 170 175

Leu Thr Ser Glu Ser Gln Leu Thr Ile Thr Lys Glu Lys Lys Glu Glu 180 185 190 W

Leu Gln Asp Cys Lys Ile Ser Pro Leu Met Val Ala Tyr Met Leu Glu 200 205 Arg Glu Leu Val Arg Lys Thr Arg Phe Leu Pro Val Ala Gly Gly Thr Ser Ser Val Tyr Ile Glu Val Leu His Leu Thr Gln Gly Thr Cys Trp Glu Gln Met Tyr Thr Pro Gly Gly Glu Val Arg Asn Asp Asp Val Asp 245 250 Gln Ser Leu Ile Ile Ala Ala Arg Ser Ile Val Arg Arg Ala Ala Val 265 Ser Ala Asp Pro Leu Ala Ser Leu Leu Glu Met Cys His Ser Thr Gln 275 280 285 Ile Gly Gly Thr Arg Met Val Asp Ile Leu Arg Gln Asn Pro Thr Glu 295 300 Glu Gln Ala Val Glu Ile Cys Lys Ala Ala Met Gly Leu Arg Ile Ser Ser Ser Phe Ser Phe Gly Gly Phe Thr Phe Lys Arg Thr Ser Gly Ser 335 330 Ser Val Lys Arg Glu Glu Glu Val Leu Thr Gly Asn Leu Gln Thr Leu 345 Lys Ile Arg Val His Glu Gly Tyr Glu Glu Phe Thr Met Val Gly Lys 360 Arg Ala Thr Ala Ile Leu Arg Lys Ala Thr Arg Arg Leu Ile Gln Leu Ile Val Ser Gly Arg Asp Glu Gln Ser Ile Ala Glu Ala Ile Ile Val 385 Ala Met Val Phe Ser Gln Glu Asp Cys Met Ile Lys Ala Val Arg Gly 405 410 Asp Leu Asn Phe Val Asn Arg Ala Asn Gln Arg Leu Asn Pro Met His 420 425 430 Gln Leu Leu Arg His Phe Gln Lys Asp Ala Lys Val Leu Phe Gln Asn 440 435 Trp Gly Ile Glu His Ile Asp Asn Val Met Gly Met Ile Gly Val Leu 460 Pro Asp Met Thr Pro Ser Thr Glu Met Ser Met Arg Gly Val Arg Val 470 475 480 Ser Lys Met Gly Val Asp Glu Tyr Ser Ser Ala Glu Arg Val Val Val

485

(i)

490

495

Ser Ile Asp Arg Phe Leu Arg Val Arg Asp Gln Arg Gly Asn Val Leu 510 500 505 Leu Ser Pro Glu Glu Val Ser Glu Thr Gln Gly Thr Glu Lys Leu Thr Ile Thr Tyr Ser Ser Ser Met Met Trp Glu Ile Asn Gly Pro Glu Ser Val Leu Val Asn Thr Tyr Gln Trp Ile Ile Arg Asn Trp Glu Thr Val 545 555 560 Lys Ile Gin Trp Ser Gin Asn Pro Thr Met Leu Tyr Asn Lys Met Giu 570 Phe Glu Pro Phe Gln Ser Leu Val Pro Lys Ala Ile Arg Gly Gln Tyr 585 Ser Gly Phe Val Arg Thr Leu Phe Gln Gln Met Arg Asp Val Leu Gly ഡെ Thr Phe Asp Thr Thr Gln Ile Ile Lys Leu Leu Pro Phe Ala Ala Ala 615 620 Pro Pro Lys Gln Ser Arg Met Gln Phe Ser Ser Leu Thr Val Asn Val 630 635 Arg Gly Ser Gly Met Arg Ile Leu Val Arg Gly Asn Ser Pro Ile Phe Asn Tyr Asn Lys Thr Thr Lys Arg Leu Thr Ile Leu Gly Lys Asp Ala Gly Thr Leu Thr Glu Asp Pro Asp Glu Gly Thr Ser Gly Val Glu Ser 680 685 Ala Val Leu Arg Gly Phe Leu Ile Leu Gly Lys Glu Asp Arg Arg Tyr 690 695 Gly Pro Ala Leu Ser Ile Asn Glu Leu Ser Asn Leu Ala Lys Gly Glu Lys Ala Asn Val Leu Ile Gly Gln Gly Asp Val Val Leu Val Met Lys 725 730 735 Arg Lys Arg Asn Ser Ser Ile Leu Thr Asp Ser Gln Thr Ala Thr Lys 745 Arg Ile Arg Met Ala Ile Asn 755

(2) INFORMATION FOR SEQ ID NO:31:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2341 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: wild type A/Ann Arbor/6/60 (H2N2) Egg Passage 2(3)
- (vii) IMMEDIATE SOURCE:
 - (B) CLONE: PB1
- (ix) FEATURE:
 - (A) NAME/KEY: conflict
 - (B) LOCATION: replace(123, "g")
 - (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])
- (ix) FEATURE:
 - (A) NAME/KEY: conflict
 - (B) LOCATION: replace(486, "u")
 - (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3); c in 1988 reported wild type E28-32 strain" /citation= ([1][2])
- (ix) FEATURE:
 - (A) NAME/KEY: conflict
 - (B) LOCATION: replace(1195, "g")

41)

(D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: mutation
- (B) LOCATION: replace(1276, "a")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain; a in wt2(3); g in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1395, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3); g in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1766, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(2005, "a")
- (D) OTHER INFORMATION: /note= "a in ca "master" strain and in wt2(3); g in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(2019, "u")
- (D) OTHER INFORMATION: /note= "u in ca "master" strain and in wt2(3); c in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 25..2295
- (D) OTHER INFORMATION: /product= "polymerase basic 1" /gene= "PB1" /note= "polymerase basic 1" /citation= ([1][2])

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G
- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA
- (G) DATE: 1993
- (K) RELEVANT RESIDUES IN SEQ ID NO:31: FROM 1 TO 2341

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Cox, N J
 Kitame, F
 Kendal, A P
 Maassab, H F
 Naeve, C
- (B) TITLE: Identification of sequence changes in the cold-adapted live attenuated influenza vaccine strain
- (C) JOURNAL: Virology
- (D) VOLUME: 167
- (F) PAGES: 554-567

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(G) DATE: 1988

(K) RELEVANT RESIDUES IN SEQ ID NO:31: FROM 1 TO 2341

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

| • | | GUC AAU CCG ACC UUA CUU UUC Val Asn Pro Thr Leu Leu Phe 5 | |
|---|-------------------|---|---|
| | | A AGU ACU ACA UUC CCU UAU AC Ser Thr Thr Phe Pro Tyr Th 20 2 | |
| | r Ser His Gly Thr | A GGA ACA GGA UAC ACC AUG GA Gly Thr Gly Tyr Thr Met As 35 40 | |
| | | A GAA AAG GGG AAG UGG ACA AC Glu Lys Gly Lys Trp Thr Th 55 | |
| | | J AAC CCA AUU GAU GGA CCA CU I Asn Pro Ile Asp Gly Pro Le 70 | |
| | | J GCA CAA ACA GAC UGC GUC CU Ala Gln Thr Asp Cys Val Le 85 | |
| | | C CAC CCA GGA AUC UUU GAA AA His Pro Gly Ile Phe Glu As 100 | n |
| | r Met Glu Val Ile | J CAA CAA ACA AGA GUG GAC AA Gln Gln Thr Arg Val Asp Ly 115 | |
| | | U UGG ACA UUG AAC AGA AAU CA Trp Thr Leu Asn Arg Asn Gl 135 | |
| | | J AUA GAG GUC UUC AGA UCG AA · Ile Glu Val Phe Arg Ser As 150 | |
| | | CUA AUA GAU UUC CUC AAG GA Leu Ile Asp Phe Leu Lys As 165 | |
| | | AUG GAA AUC ACA ACA CAC UU Met Glu Ile Thr Thr His Ph 180 18 | e |

| CAA | AGA | AAA | AGA | AGA | GUA | AGA | GAC | AÀC | AUG | ACC | AAG | AAA | AUG | GUC | ACA | 627 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------------|-----|------|
| | | | | | | | | | | | | | | Va1 200 | | 027 |
| | | | | | | | | | | | | | | AGC Ser | | 675 |
| | | | | | | | | | | | | | | GAG Glu | | 723 |
| | | | | | | | | | | | | | | AUC Ile | | 771 |
| | | | | | | | | | | | | | | GAG Glu | | 819 |
| | | | | | | | | | | | | | | GCU A1a 280 | | 867 |
| | | | | | | | | | | | | | | ACA Thr | | 915 |
| | | | | | | | | | | | | | | AAU Asn | | 963 |
| | | | | | | | | | | | | | | AAU Asn | | 1011 |
| | | | | | | | | | | | | | | UUC Phe | | 1059 |
| | | | | | | | | | | | | | | AAG Lys 360 | | 1107 |
| | | | | | | | | | | | | | | AUU Ile | | 1155 |
| | | | | | | | | | | | | | | AUA Ile | | 1203 |
| | | | | | | | | | | | | | | AUG Met | | 1251 |

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| | AUG Met | | | | | | | | 1299 |
|--|-------------------|--|--|--|--|--|--|--------------|------|
| | GGA Gly | | | | | | | | 1347 |
| | UCC Ser | | | | | | | | 1395 |
| | AUA Ile | | | | | | | | 1443 |
| | AUC Ile 475 | | | | | | | | 1491 |
| | GAA Glu | | | | | | | | 1539 |
| | AUG Met | | | | | | | GCU - Ala | 1587 |
| | AUG Met | | | | | | | | 1635 |
| | CUU Leu | | | | | | | | 1683 |
| | UAC Tyr 555 | | | | | | | | 1731 |
| | AGG Arg | | | | | | | | 1779 |
| | GCA Ala | | | | | | | | 1827 |
| | AAU Asn | | | | | | | | 1875 |
| | GAC Asp | | | | | | | | 1923 |

6

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 757 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

Met Asp Val Asn Pro Thr Leu Leu Phe Leu Lys Val Pro Ala Gln Asn 1 5 10 15

Ala Ile Ser Thr Thr Phe Pro Tyr Thr Gly Asp Pro Pro Tyr Ser His

6

Gly Thr Gly Thr Gly Tyr Thr Met Asp Thr Val Asn Arg Thr His Gln 35 Tyr Ser Glu Lys Gly Lys Trp Thr Thr Asn Thr Glu Thr Gly Ala His Gln Leu Asn Pro Ile Asp Gly Pro Leu Pro Glu Asp Asn Glu Pro Ser Gly Tyr Ala Gln Thr Asp Cys Val Leu Glu Ala Met Ala Phe Leu Glu 85 Glu Ser His Pro Gly Ile Phe Glu Asn Ser Cys Leu Glu Thr Met Glu 105 Val Ile Gln Gln Thr Arg Val Asp Lys Leu Thr Gln Gly Arg Gln Thr 120 Tyr Asp Trp Thr Leu Asn Arg Asn Gln Pro Ala Ala Thr Ala Leu Ala 130 135 Asn Thr Ile Glu Val Phe Arg Ser Asn Gly Leu Thr Ala Asn Glu Ser 150 Gly Arg Leu Ile Asp Phe Leu Lys Asp Val Ile Glu Ser Met Asp Lys 170 Glu Glu Met Glu Ile Thr Thr His Phe Gln Arg Lys Arg Arg Val Arg 180 Asp Asn Met Thr Lys Lys Met Val Thr Gln Arg Thr Ile Gly Lys Lys Lys Gln Arg Leu Asn Lys Arg Ser Tyr Leu Ile Arg Ala Leu Thr Leu 220 Asn Thr Met Thr Lys Asp Ala Glu Arg Gly Lys Leu Lys Arg Arg Ala 225 230 Ile Ala Thr Pro Gly Met Gln Ile Arg Gly Phe Val Tyr Phe Val Glu 250 Thr Leu Ala Arg Ser Ile Cys Glu Lys Leu Glu Gln Ser Gly Leu Pro 270 260 265 Val Gly Gly Asn Glu Lys Lys Ala Lys Leu Ala Asn Val Val Arg Lys Met Met Thr Asn Ser Gln Asp Thr Glu Leu Ser Phe Thr Ile Thr Gly Asp Asn Thr Lys Trp Asn Glu Asn Gln Asn Pro Arg Met Phe Leu Ala 305 310 315 320

Met Ile Thr Tyr Ile Thr Arg Asn Gln Pro Glu Trp Phe Arg Asn Val Leu Ser Ile Ala Pro Ile Met Phe Ser Asn Lys Met Ala Arg Leu Gly Lys Gly Tyr Met Phe Lys Ser Lys Ser Met Lys Leu Arg Thr Gln Ile 360 Pro Ala Glu Met Leu Ala Ser Ile Asp Leu Lys Tyr Phe Asn Glu Ser 370 Thr Arg Lys Lys Ile Glu Glu Ile Arg Pro Leu Leu Ile Asp Gly Thr 390 Val Ser Leu Ser Pro Gly Met Met Gly Met Phe Asn Met Leu Ser 410 Thr Ile Leu Gly Val Ser Ile Leu Asn Leu Gly Gln Lys Lys Tyr Thr 420 Lys Thr Thr Tyr Trp Trp Asp Gly Leu Gln Ser Ser Asp Asp Phe Ala Leu Ile Val Asn Ala Pro Asn His Asp Gly Ile Gln Ala Gly Val Asp 450 Arg Phe Tyr Arg Thr Cys Lys Leu Val Gly Ile Asn Met Ser Lys Lys 465 Lys Ser Tyr Ile Asn Arg Thr Gly Thr Phe Glu Phe Thr Ser Phe Phe 490 Tyr Arg Tyr Gly Phe Val Ala Asn Phe Ser Met Glu Leu Pro Ser Phe 500 510 Gly Val Ser Gly Ile Asn Glu Ser Ala Asp Met Ser Ile Gly Val Thr 515 520 Val Ile Lys Asn Asn Met Ile Asn Asn Asp Leu Gly Pro Ala Thr Ala 540 Gln Leu Ala Leu Gln Leu Phe Ile Lys Asp Tyr Arg Tyr Thr Tyr Arg 545 555 Cys His Arg Gly Asp Thr Gln Ile Gln Thr Arg Arg Ser Phe Glu Leu 565 570 Lys Lys Leu Trp Gly Gln Thr Arg Ser Lys Ala Gly Leu Leu Val Ser Asp Gly Gly Pro Asn Leu Tyr Asn Ile Arg Asn Leu His Ile Pro Glu 595 Val Cys Leu Lys Trp Glu Leu Met Asp Glu Asp Tyr Gln Gly Arg Leu 610

615

620

Cys Asn Pro Leu Asn Pro Phe Val Ser His Lys Glu Ile Glu Ser Val 625 630 635 640

Asn Asn Ala Val Val Met Pro Ala His Gly Pro Ala Lys Ser Met Glu 645 650 655

Tyr Asp Ala Val Thr Thr His Ser Trp Ile Pro Lys Arg Asn Arg
660 665 670

Ser Ile Leu Asn Thr Ser Gln Arg Gly Ile Leu Glu Asp Glu Gln Met 675 680 685

Tyr Gln Lys Cys Cys Asn Leu Phe Glu Lys Phe Phe Pro Ser Ser Ser 690 695 700

Tyr Arg Arg Pro Val Gly Ile Ser Ser Met Val Glu Ala Met Val Ser 705 710 715 720

Arg Ala Arg Ile Asp Ala Arg Ile Asp Phe Glu Ser Gly Arg Ile Lys
725 730 735

Lys Glu Glu Phe Ala Glu Ile Met Lys Ile Cys Ser Thr Ile Glu Glu 740 745 750

Leu Arg Arg Gln Lys 755

(2) INFORMATION FOR SEQ ID NO:33:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2233 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: wild type A/Ann Arbor/6/60 (H2N2) Egg Passage 2(3)

(vii) IMMEDIATE SOURCE:

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(B) CLONE: PA

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(20, "c")
- (D) OTHER INFORMATION: /note= "c in ca "master" strain and in wt2(3); u in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(75, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); u in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1861, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(2167..2168, "cc")
- (D) OTHER INFORMATION: /note= "cc in ca "master" strain and in wt2(3); uu in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 25..2172

(D) OTHER INFORMATION: /product= "polymerase acidic protein"

/gene= "PA"

/note= "polymerase acidic protein"

/citation= ([1][2])

(x) PUBLICATION INFORMATION:

(A) AUTHORS: Herlocher, M L

Maassab, H F Webster, R G

(B) TITLE: Molecular and biological changes in the cold adapted

master strain A/AA/6/60 (H2N2) influenza virus

(C) JOURNAL: Proceedings of the National Academy of Sciences of

the USA

(G) DATE: 1993

(K) RELEVANT RESIDUES IN SEQ ID NO:33: FROM 1 TO 2233

(x) PUBLICATION INFORMATION:

(A) AUTHORS: Cox, N J

Kitame, F Kendal, A P Maassab, H F Naeve, C

(B) TITLE: Identification of sequence changes in the cold-adapted

live attenuated influenza strain, A/Ann

Arbor/6/60(H2N2)

(C) JOURNAL: Virology

(D) VOLUME: 167

(F) PAGES: 554-567

(G) DATE: 1988

(K) RELEVANT RESIDUES IN SEQ ID NO:33: FROM 1 TO 2233

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

AGCGAAAGCA GGUACUGAUC CGAA AUG GAA GAU UUU GUG CGA CAA UGC UUC

Met Glu Asp Phe Val Arg Gln Cys Phe

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51

Asn Pro Met Ile Val Glu Leu Ala Glu Lys Ala Met Lys Glu Tyr Gly 10 GAG GAU CUG AAA AUC GAA ACA AAC AAA UUU GCA GCA AUA UGC ACU CAC 147 Glu Asp Leu Lys Ile Glu Thr Asn Lys Phe Ala Ala Ile Cys Thr His 30 UUG GAA GUA UGC UUC AUG UAU UCA GAU UUU CAU UUC AUC AAU GAG CAA 195 Leu Glu Val Cys Phe Met Tyr Ser Asp Phe His Phe Ile Asn Glu Gln 45 50 GGC GAG UCA AUA AUA GUA GAG CUU GAU GAU CCA AAU GCA CUU UUG AAG 243 Gly Glu Ser Ile Ile Val Glu Leu Asp Asp Pro Asn Ala Leu Leu Lys 65 CAC AGA UUU GAA AUA AUA GAG GGA AGA GAU CGC ACA AUG GCC UGG ACA 291 His Arg Phe Glu Ile Ile Glu Gly Arg Asp Arg Thr Met Ala Trp Thr GUA GUA AAC AGU AUU UGC AAC ACU ACA GGA GCU GAG AAA CCG AAG UUU 339 Val Val Asn Ser Ile Cys Asn Thr Thr Gly Ala Glu Lys Pro Lys Phe 90 CUG CCA GAU UUG UAU GAU UAC AAG GAG AAU AGA UUC AUC GAG AUU GGA 387 Leu Pro Asp Leu Tyr Asp Tyr Lys Glu Asn Arg Phe Ile Glu Ile Gly 110 115 GUG ACA AGG AGG GAA GUC CAC AUA UAC UAU CUU GAA AAG GCC AAU AAA 435 Val Thr Arg Arg Glu Val His Ile Tyr Tyr Leu Glu Lys Ala Asn Lys 125 130 AUU AAA UCU GAG AAG ACA CAC AUC CAC AUU UUC UCA UUC ACU GGG GAA 483 Ile Lys Ser Glu Lys Thr His Ile His Ile Phe Ser Phe Thr Gly Glu 145 GAA AUG GCC ACA AAG GCC GAC UAC ACU CUC GAU GAG GAA AGC AGG GCU 531 Glu Met Ala Thr Lys Ala Asp Tyr Thr Leu Asp Glu Glu Ser Arg Ala 155 160 AGG AUC AAA ACC AGA CUA UUC ACC AUA AGA CAA GAA AUG GCU AGC AGA 579 Arg Ile Lys Thr Arg Leu Phe Thr Ile Arg Gln Glu Met Ala Ser Arg 170 185 GGC CUC UGG GAU UCC UUU CAU CAG UCC GAA AGA GGC GAA GAA ACA AUU 627 Gly Leu Trp Asp Ser Phe His Gln Ser Glu Arg Gly Glu Glu Thr Ile 200 190 GAA GAA AGA UUU GAA AUC ACA GGG ACA AUG CGC AGG CUC GCC GAC CAA 675 Glu Glu Arg Phe Glu Ile Thr Gly Thr Met Arg Arg Leu Ala Asp Gln 210 AGU CUC CCG CCG AAC UUC UCC UGC CUU GAG AAU UUU AGA GCC UAU GUG 723 Ser Leu Pro Pro Asn Phe Ser Cys Leu Glu Asn Phe Arg Ala Tyr Val 220 225 230

W

| | | | | | | | CAA Gln | 771 |
|--|---|------|-------|------|------|--|-------------------|------|
| | | | | | | | ACA Thr | 819 |
| | | | | | | | UCC Ser 280 | 867 |
| | | | | | | | AGU Ser | 915 |
| | | | | | | | AGA Arg | 963 |
| | | | | | | | AAG Lys | 1011 |
| | | | | | | | GAA G1u | 1059 |
| | | | | | | | AUG Met 360 | 1107 |
| | | | | | | | CCA Pro | 1155 |
| | | | | | | | CAA Gln | 1203 |
| | | | | | | | CAG G1n | 1251 |
| | _ | | _ | | | | GAG Glu | 1299 |
| | | | | | | | AGC Ser 440 | 1347 |
| | | | | | | | ACA Thr | 1395 |

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UAU AUA AUG AAG GGG GUA UAC AUU AAU ACU GCC UUG CUU AAU GCA UCC Tyr Ile Met Lys Gly Val Tyr Ile Asn Thr Ala Leu Leu Asn Ala Ser UGU GCA GCA AUG GAC GAU UUC CAA CUA AUU CCC AUG AUA AGC AAA UGU Cys Ala Ala Met Asp Asp Phe Gln Leu Ile Pro Met Ile Ser Lys Cys AGA ACU AAA GAG GGA AGG CGA AAG ACC AAU UUA UAU GGU UUC AUC AUA Arg Thr Lys Glu Gly Arg Arg Lys Thr Asn Leu Tyr Gly Phe Ile Ile AAA GGA AGA UCU CAC UUA AGG AAU GAC ACC GAC GUG GUA AAC UUU GUG Lys Gly Arg Ser His Leu Arg Asn Asp Thr Asp Val Val Asn Phe Val AGC AUG GAG UUU UCU CUC ACU GAC CCA AGA CUU GAG CCA CAC AAA UGG Ser Met Glu Phe Ser Leu Thr Asp Pro Arg Leu Glu Pro His Lys Trp GAG AAG UAC UGU GUU CUU GAG AUA GGA GAU AUG CUA CUA AGA AGU GCC Glu Lys Tyr Cys Val Leu Glu Ile Gly Asp Met Leu Leu Arg Ser Ala AUA GGC CAG GUG UCA AGG CCC AUG UUC UUG UAU GUG AGG ACA AAU GGA Ile Gly Gln Val Ser Arg Pro Met Phe Leu Tyr Val Arg Thr Asn Gly ACA UCA AAG AUU AAA AUG AAA UGG GGA AUG GAG AUG AGG CGU UGC CUC Thr Ser Lys Ile Lys Met Lys Trp Gly Met Glu Met Arg Arg Cys Leu CUU CAG UCA CUC CAA CAA AUC GAG AGU AUG AUU GAA GCC GAG UCC UCU Leu Gln Ser Leu Gln Gln Ile Glu Ser Met Ile Glu Ala Glu Ser Ser GUC AAG GAG AAA GAC AUG ACC AAA GAG UUU UUC GAG AAU AAA UCA GAA Val Lys Glu Lys Asp Met Thr Lys Glu Phe Phe Glu Asn Lys Ser Glu ACA UGG CCC AUU GGA GAG UCC CCC AAA GGA GUG GAA GAA GGU UCC AUU Thr Trp Pro Ile Gly Glu Ser Pro Lys Gly Val Glu Glu Gly Ser Ile GGG AAG GUC UGC AGG ACU UUA UUA GCC AAG UCG GUA UUC AAU AGC CUG Gly Lys Val Cys Arg Thr Leu Leu Ala Lys Ser Val Phe Asn Ser Leu UAU GCA UCU CCA CAA UUA GAA GGA UUU UCA GCU GAA UCA AGA AAA CUG Tyr Ala Ser Pro Gln Leu Glu Gly Phe Ser Ala Glu Ser Arg Lys Leu CUU CUU GUC GUU CAG GCU CUU AGG GAC AAU CUU GAA CCU GGG ACC UUU Leu Leu Val Val Gln Ala Leu Arg Asp Asn Leu Glu Pro Gly Thr Phe

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| | | | GGG Gly 685 | | | | | | | | | | | | | 2115 |
|-----------|-------------------|-------------------|-------------------|-----------|-----------|-----------|-------------------|------------|-----------|-----------|-----------|------------|------------|-----------|-----------|------|
| | | | UUG Leu | | | | | | | | | | | | | 2163 |
| | CCA Pro 715 | | UAGU | JUGU | GGC / | AAUGO | CUACI | JA Ul | JUGCI | JAUCO | AUA | ACUGI | JCCA | | | 2212 |
| AAA | \AGU/ | ACC I | JUGUL | JUCUA | AC U | | | | | | | | | | | 2233 |
| (2) | INFO |)rma ⁻ | rion | FOR | SEQ | ID I | VO:34 | 1: | | | | | | | | |
| | (| (i) : | SEQUE | ENCE | CHAI | RACTI | ERIS | TICS | : | | | | | | | |
| | | | (A) | LEI | NGTH | : 716 | 5 am | ino a | acid | S | | | | | | |
| | | | (B) | TYI | PE: a | amino | o ac | i d | | | | | | | | |
| | | | (D) |) TOI | POL00 | GY: | linea | ar | | | | | | | | |
| | (f | ii) 1 | MOLE | CULE | TYP | E: pi | rote [.] | in | | | | | | | • | |
| | • | • | | | | • | | | | | | | | | | |
| | () | ci) : | SEQUE | ENCE | DES | CRIP | TION | : SE | Q ID | NO:3 | 34: | | | | | |
| Met 1 | Glu | Asp | Phe | Val 5 | Arg | Gln | Cys | Phe | Asn 10 | Pro | Met | Ile | Val | Glu 15 | Leu | |
| Ala | Glu | Lys | A1 a 20 | Met | Lys | Glu | Tyr | G1y 25 | Glu | Asp | Leu | Lys | Ile 30 | Glu | Thr | |
| Asn | Lys | | Ala | | | | | | | | | | | Met | Tyr | |
| Ser | Asp 50 | Phe | His | Phe | Ile | Asn 55 | G1 u | Gln | Gly | Glu | Ser 60 | Ile | Ile | Val | Glu | |
| Leu 65 | Asp | Asp | Pro | Asn | A1a 70 | Leu | Leu | Lys | His | Arg 75 | Phe | Glu | Ile | Ile | G1u 80 | |
| Gly | Arg | Asp | Arg | Thr 85 | Met | Ala | Trp | Thr | Va1 90 | Val | Asn | Ser | Ile | Cys 95 | Asn | |
| Thr | Thr | Gly | Ala 100 | G1 u | Lys | Pro | Lys | Phe 105 | Leu | Pro | Asp | Leu | Tyr 110 | Asp | Tyr | |
| Lys | Glu | Asn 115 | Arg | Phe | Ile | Glu | Ile 120 | Gly | Val | Thr | Arg | Arg 125 | Glu | Val | His | |

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Ile Tyr Tyr Leu Glu Lys Ala Asn Lys Ile Lys Ser Glu Lys Thr His Ile His Ile Phe Ser Phe Thr Gly Glu Glu Met Ala Thr Lys Ala Asp Tyr Thr Leu Asp Glu Glu Ser Arg Ala Arg Ile Lys Thr Arg Leu Phe Thr Ile Arg Gln Glu Met Ala Ser Arg Gly Leu Trp Asp Ser Phe His Gln Ser Glu Arg Gly Glu Glu Thr Ile Glu Glu Arg Phe Glu Ile Thr Gly Thr Met Arg Arg Leu Ala Asp Gln Ser Leu Pro Pro Asn Phe Ser 220 Cys Leu Glu Asn Phe Arg Ala Tyr Val Asp Gly Phe Glu Pro Asn Gly Tyr Ile Glu Gly Lys Leu Ser Gln Met Ser Lys Glu Val Asn Ala Lys Ile Glu Pro Phe Leu Lys Thr Thr Pro Arg Pro Ile Arg Leu Pro Asp 270 Gly Pro Pro Cys Ser Gln Arg Ser Lys Phe Leu Leu Met Asp Ala Leu Lys Leu Ser Ile Glu Asp Pro Ser His Glu Gly Glu Gly Ile Pro Leu Tyr Asp Ala Ile Lys Cys Met Arg Thr Phe Phe Gly Trp Lys Glu Pro 320 Tyr Val Val Lys Pro His Glu Lys Gly Ile Asn Pro Asn Tyr Leu Leu Ser Trp Lys Gln Val Leu Ala Glu Leu Gln Asp Ile Glu Asn Glu Glu Lys Ile Pro Arg Thr Lys Asn Met Lys Lys Thr Ser Gln Leu Lys Trp Ala Leu Gly Glu Asn Met Ala Pro Glu Lys Val Asp Phe Asp Asp Cys 380 Arg Asp Val Ser Asp Leu Lys Gln Tyr Asp Ser Asp Glu Pro Glu Leu 390 395 Arg Ser Leu Ser Ser Trp Ile Gln Asn Glu Phe Asn Lys Ala Cys Glu 415 Leu Thr Asp Ser Ile Trp Ile Glu Leu Asp Glu Ile Gly Glu Asp Val

420

425

430

Ala Pro Ile Glu His Ile Ala Ser Met Arg Arg Asn Tyr Phe Thr Ala 435 440 445 Glu Val Ser His Cys Arg Ala Thr Glu Tyr Ile Met Lys Gly Val Tyr Ile Asn Thr Ala Leu Leu Asn Ala Ser Cys Ala Ala Met Asp Asp Phe Gln Leu Ile Pro Met Ile Ser Lys Cys Arg Thr Lys Glu Gly Arg Arg Lys Thr Asn Leu Tyr Gly Phe Ile Ile Lys Gly Arg Ser His Leu Arg Asn Asp Thr Asp Val Val Asn Phe Val Ser Met Glu Phe Ser Leu Thr 520 Asp Pro Arg Leu Glu Pro His Lys Trp Glu Lys Tyr Cys Val Leu Glu 530 Ile Gly Asp Met Leu Leu Arg Ser Ala Ile Gly Gln Val Ser Arg Pro 550 Met Phe Leu Tyr Val Arg Thr Asn Gly Thr Ser Lys Ile Lys Met Lys 570 Trp Gly Met Glu Met Arg Arg Cys Leu Leu Gln Ser Leu Gln Gln Ile 580 585 Glu Ser Met Ile Glu Ala Glu Ser Ser Val Lys Glu Lys Asp Met Thr Lys Glu Phe Phe Glu Asn Lys Ser Glu Thr Trp Pro Ile Gly Glu Ser 615 620 Pro Lys Gly Val Glu Glu Gly Ser Ile Gly Lys Val Cys Arg Thr Leu 625 630 Leu Ala Lys Ser Val Phe Asn Ser Leu Tyr Ala Ser Pro Gln Leu Glu 650 Gly Phe Ser Ala Glu Ser Arg Lys Leu Leu Leu Val Val Gln Ala Leu 670 660 665 Arg Asp Asn Leu Glu Pro Gly Thr Phe Asp Leu Gly Gly Leu Tyr Glu 680 Ala Ile Glu Glu Cys Leu Ile Asn Asp Pro Trp Val Leu Leu Asn Ala 695 700 Ser Trp Phe Asn Ser Phe Leu Thr His Ala Pro Arg 705 715

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- (2) INFORMATION FOR SEQ ID NO:35:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1773 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: RNA (genomic)
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: wild type A/Ann Arbor/6/60 (H2N2) Egg Passage 2(3)
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: HA
 - (ix) FEATURE:
 - (A) NAME/KEY: mutation
 - (B) LOCATION: replace(144, "a")
 - (ix) FEATURE:
 - (A) NAME/KEY: mutation
 - (ix) FEATURE:
 - (A) NAME/KEY: mutation

| (B) L | OCATION: replace(7 | '29, "a") | |
|-----------------|--|---|-------------------|
| (D) O | THER INFORMATION: | /gene= "HA" /note= "c in ca "master wt2(3)" /citation= ([1]) | " strain; a in |
| (ix) FEATUR | E: | | |
| (A) N | AME/KEY: CDS | | |
| (B) L | OCATION: 441729 | | |
| (D) 0 | THER INFORMATION: | <pre>/product= "hemagglutini /gene= "HA" /note= "hemagglutinin p /citation= ([1])</pre> | |
| (x) PUBLIC | ATION INFORMATION: | | |
| (A) A | UTHORS: Herlocher, Maassab, H Webster, F | l F | |
| (B) T | | nd biological changes in n A/AA/6/60 (H2N2) infl | |
| (C) J | OURNAL: Proceeding the USA | s of the National Acade | my of Sciences of |
| (G) D | ATE: 1993 | | |
| (K) R | ELEVANT RESIDUES 1 | N SEQ ID NO:35: FROM 1 | TO 1773 |
| (xi) SEQUEN | CE DESCRIPTION: SE | Q ID NO:35: | |
| AGCAAAAGCA GGGG | UUAUAC CAUAGACAAC | CAAAAGCAAA ACA AUG GCC Met Ala 1 | |
| | | GUG AGA GGG GAC AAG AUA Val Arg Gly Asp Lys Ile 15 | |
| | | AG ACG GUC GAC ACA AAU ilu Thr Val Asp Thr Asn 30 | |
| | Val Thr His Ala L | AG GAC AUU CUU GAG AAG ys Asp Ile Leu Glu Lys 45 50 | |

| _ | - | | | | | CCU Pro | | | | 247 |
|---|---|--|--|--|--|-------------------|--|--|--|-----|
| | | | | | | AAU Asn | | | | 295 |
| | | | | | | AUG Met 95 | | | | 343 |
| | | | | | | AAU Asn | | | | 391 |
| | | | | | | GAG Glu | | | | 439 |
| | | | | | | ACU Thr | | | | 487 |
| | | | | | | AGG Arg | | | | 535 |
| | | | | | | AAA Lys 175 | | | | 583 |
| | | | | | | GGG Gly | | | | 631 |
| | | | | | | AAU Asn | | | | 679 |
| | | | | | | UCA Ser | | | | 727 |
| | | | | | | AGA Arg | | | | 775 |
| | | | | | | UUU Phe 255 | | | | 823 |
| | | | | | | UCG Ser | | | | 871 |

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GGG AUC AUG AAA ACA GAA GGA ACA CUU GAG AAC UGU GAG ACC AAA UGC Gly Ile Met Lys Thr Glu Gly Thr Leu Glu Asn Cys Glu Thr Lys Cys CAA ACU CCU UUG GGA GCA AUA AAU ACA ACA UUG CCU UUU CAC AAU GUC Gln Thr Pro Leu Gly Ala Ile Asn Thr Thr Leu Pro Phe His Asn Val CAC CCA CUG ACA AUA GGU GAG UGC CCC AAA UAU GUA AAA UCG GAG AAG His Pro Leu Thr Ile Gly Glu Cys Pro Lys Tyr Val Lys Ser Glu Lys UUG GUC UUA GCA ACA GGA CUA AGG AAU GUU CCC CAG AUU GAA UCA AGA Leu Val Leu Ala Thr Gly Leu Arg Asn Val Pro Gln Ile Glu Ser Arg GGA UUG UUU GGG GCA AUA GCU GGU UUU AUA GAA GGA GGA UGG CAA GGA Gly Leu Phe Gly Ala Ile Ala Gly Phe Ile Glu Gly Gly Trp Gln Gly AUG GUU GAU GGU UGG UAU GGA UAC CAU CAC AGC AAU GAC CAG GGA UCA Met Val Asp Gly Trp Tyr Gly Tyr His His Ser Asn Asp Gln Gly Ser GGG UAU GCA GCA GAC AAA GAA UCC ACU CAA AAG GCA UUU GAU GGA AUC Gly Tyr Ala Ala Asp Lys Glu Ser Thr Gln Lys Ala Phe Asp Gly Ile ACC AAC AAG GUA AAU UCU GUG AUU GAA AAG AUA AAC ACC CAA UUU GAA Thr Asn Lys Val Asn Ser Val Ile Glu Lys Ile Asn Thr Gln Phe Glu GCU GUU GGG AAA GAA UUC AGU AAC UUA GAG AGA AGA CUG GAG AAC UUG Ala Val Gly Lys Glu Phe Ser Asn Leu Glu Arg Arg Leu Glu Asn Leu AAC AAA AAG AUG GAA GAC GGG UUU CUA GAU GUG UGG ACA UAC AAU GCU Asn Lys Lys Met Glu Asp Gly Phe Leu Asp Val Trp Thr Tyr Asn Ala GAG CUU CUA GUU CUG AUG GAA AAU GAG AGG ACA CUU GAC UUU CAU GAU Glu Leu Leu Val Leu Met Glu Asn Glu Arg Thr Leu Asp Phe His Asp UCU AAU GUC AAG AAU CUG UAU GAU AAA GUC AGA AUG CAG CUG AGG GAC Ser Asn Val Lys Asn Leu Tyr Asp Lys Val Arg Met Gln Leu Arg Asp AAC GUC AAA GAA CUA GGA AAU GGA UGU UUU GAA UUU UAU CAC AAA UGU Asn Val Lys Glu Leu Gly Asn Gly Cys Phe Glu Phe Tyr His Lys Cys GAU GAU GAA UGC AUG AAU AGU GUG AAA AAC GGG ACA UAU GAU UAU CCC Asp Asp Glu Cys Met Asn Ser Val Lys Asn Gly Thr Tyr Asp Tyr Pro



| | | | | | | | | | | | | | | GGG Gly 515 | | 1591 |
|-----------|--|-----------|------------|-----------|-----------|-------------|-----------|------------|------------|-----------|-----------|-----------|------------|-------------------|-----------|------|
| | | | | | | | | | | | | | | GCU Ala | | 1639 |
| | | | | | | | | | | | | | | UCU Ser | | 1687 |
| | | | | | | | | | UGC Cys | | | | | | | 1729 |
| UGA | JUAU | AAG (| JCAU | JUUAI | JA Al | JUAA | AAACA | A CC | CUUGI | JUUC | UACI | j | | | | 1773 |
| (2) | INFO | ORMA | FION | FOR | SEQ | ID I | NO:36 | 5: | | | | | | | | |
| | (| (i) \$ | SEQUE | ENCE | CHA | RACTI | ERIS | TICS | : | | | | | | | |
| | | | (A) | LEI | NGTH: | : 562 | 2 ami | ino a | acid | 5 | | | | | | |
| | | | (B) | TYI | PE: a | amino | aci | i d | | | | | | | | |
| | | | (D) | TOI | POLO(| GY: | linea | ar | | | | | | | | |
| | (A) LENGTH: 562 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (xi) SEQUENCE DESCRIPTION: SEQ ID NO:36: | | | | | | | | | | | | | | | |
| | () | ki) S | SEQU | ENCE | DES | CRIP | TION: | : SE | Q ID | NO:3 | 36: | | | | | |
| Met 1 | Ala | Ile | Ile | Tyr 5 | Leu | Ile | Leu | Leu | Phe 10 | Thr | Ala | Val | Arg | Gly 15 | Asp | |
| Lys | Ile | Cys | Ile 20 | Gly | Tyr | His | Ala | Asn 25 | Asn | Ser | Thr | Glu | Thr 30 | Val | Asp | |
| Thr | Asn | Leu 35 | Glu | Arg | Asn | Val | Thr 40 | Va1 | Thr | His | Ala | Lys 45 | Asp | Ile | Leu | |
| Glu | Lys 50 | Thr | His | Asn | Gly | Lys 55 | Leu | Cys | Lys | Leu | Asn 60 | Gly | Ιle | Pro | Pro | |
| Leu 65 | Glu | Leu | Gly | Asp | Cys 70 | Ser | Ile | Ala | Gly | Trp 75 | Leu | Leu | Gly | Asn | Pro 80 | |
| Glu | Cys | Asp | Arg | Leu 85 | Leu | Ser | Val | Pro | G1 u 90 | Trp | Ser | Tyr | Ile | Met 95 | Glu | |
| Lys | G1 u | Asn | Pro 100 | Arg | Asn | G1 <i>y</i> | Leu | Cys 105 | Tyr | Pro | Gly | Asn | Phe 110 | Asn | Asp | |

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Tyr Glu Glu Leu Lys His Leu Leu Ser Ser Val Lys His Phe Glu Lys Val Lys Ile Leu Pro Lys Asp Arg Trp Ala Gln His Thr Thr Gly Gly Ser Gln Ala Cys Ala Val Ser Gly Asn Pro Ser Phe Phe Arg Asn 150 160 Met Val Trp Leu Thr Glu Glu Gly Ser Asn Tyr Pro Val Ala Lys Gly 165 Ser Tyr Asn Asn Thr Ser Gly Glu Gln Met Leu Ile Ile Trp Gly Val 185 His His Pro Ile Asp Glu Thr Glu Gln Arg Thr Leu Tyr Gln Asn Val 200 205 Gly Thr Tyr Val Ser Val Gly Thr Ser Thr Leu Asn Lys Arg Ser Thr 210 215 Pro Glu Ile Ala Lys Arg Pro Lys Val Asn Gly Leu Gly Ser Arg Met Glu Phe Ser Trp Thr Leu Leu Asp Met Trp Asp Thr Ile Asn Phe Glu 250 255 Ser Thr Gly Asn Leu Ile Ala Pro Glu Tyr Gly Phe Lys Ile Ser Lys Arg Gly Ser Ser Gly Ile Met Lys Thr Glu Gly Thr Leu Glu Asn Cys Glu Thr Lys Cys Gln Thr Pro Leu Gly Ala Ile Asn Thr Thr Leu Pro 290 295 Phe His Asn Val His Pro Leu Thr Ile Gly Glu Cys Pro Lys Tyr Val 305 310 Lys Ser Glu Lys Leu Val Leu Ala Thr Gly Leu Arg Asn Val Pro Gln 325 330 Ile Glu Ser Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe Ile Glu Gly 340 350 Gly Trp Gln Gly Met Val Asp Gly Trp Tyr Gly Tyr His His Ser Asn 365 Asp Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu Ser Thr Gln Lys Ala Phe Asp Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu Lys Ile Asn 390 400 Thr Gln Phe Glu Ala Val Gly Lys Glu Phe Ser Asn Leu Glu Arg Arg



405

410

415

Leu Glu Asn Leu Asn Lys Lys Met Glu Asp Gly Phe Leu Asp Val Trp
420 425 430

Thr Tyr Asn Ala Glu Leu Leu Val Leu Met Glu Asn Glu Arg Thr Leu
435 440 445

Asp Phe His Asp Ser Asn Val Lys Asn Leu Tyr Asp Lys Val Arg Met 450 455 460

Gln Leu Arg Asp Asn Val Lys Glu Leu Gly Asn Gly Cys Phe Glu Phe 465 470 475 480

Tyr His Lys Cys Asp Asp Glu Cys Met Asn Ser Val Lys Asn Gly Thr 485 490 495

Tyr Asp Tyr Pro Lys Tyr Glu Glu Glu Ser Lys Leu Asn Arg Asn Glu 500 505 510

Ile Lys Gly Val Lys Leu Ser Ser Met Gly Val Cys Arg Ile Leu Ala 515 520 525

Ile Tyr Ala Thr Val Ala Gly Ser Leu Ser Leu Ala Ile Met Met Ala 530 535 540

Gly Ile Ser Phe Trp Met Cys Ser Asn Gly Ser Leu Gln Cys Arg Ile 545 550 555 560

Cys Ile

(2) INFORMATION FOR SEQ ID NO:37:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1467 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: wild type A/Ann Arbor/6/60 (H2N2) Egg Passage 2(3)

(vii) IMMEDIATE SOURCE:

(B) CLONE: NA

(ix) FEATURE:

- (A) NAME/KEY: mutation
- (B) LOCATION: replace(394, "c")
- (D) OTHER INFORMATION: /product= "Neuraminidase"

/gene= "NA"

/note= "u in ca "master" strain; c in

wt2(3)"

/citation= ([1])

(ix) FEATURE:

- (A) NAME/KEY: mutation
- (B) LOCATION: replace(604, "a")
- (D) OTHER INFORMATION: /product= "Neuraminidase"

/gene= "NA"

/note= "u in ca "master" strain; a in

wt2(3)"

/citation= ([1])

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 20..1426
- (D) OTHER INFORMATION: /product= "neuraminidase"

/gene= "NA"

/note= "neuraminidase protein"

/citation= ([1])

(x) PUBLICATION INFORMATION:

- (A) AUTHORS: Herlocher, M L Maassab, H F Webster, R G
- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) Influenza Virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA

- (G) DATE: 1993
- (K) RELEVANT RESIDUES IN SEQ ID NO:37: FROM 1 TO 1467

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

| (XI) SEQUENCE DESCRIPTION. SEQ 10 NO.37. | | | | | | | | | | | | | | |
|---|------|--|--|--|--|--|--|--|--|--|--|--|--|--|
| AGCAAAAGCA GGAGUGAAA AUG AAU CCA AAU CAA AAG ACA AUA ACA AUU GGC Met Asn Pro Asn Gln Lys Thr Ile Thr Ile Gly 1 5 10 | | | | | | | | | | | | | | |
| UCU GUC UCU CUC ACC AUC GCA ACA GUA UGC UUC CUC AUG CAG AUU GCC Ser Val Ser Leu Thr Ile Ala Thr Val Cys Phe Leu Met Gln Ile Ala 15 20 25 | 100 | | | | | | | | | | | | | |
| AUC CUG GCA ACU ACU GUG ACA UUG CAC CUU AAG CAA CAU GAG UGC GAC Ile Leu Ala Thr Thr Val Thr Leu His Leu Lys Gln His Glu Cys Asp 30 35 40 | 148 | | | | | | | | | | | | | |
| UCC CCC GCG AGC AAC CAA GUA AUG CCA UGU GAA CCA AUA AUA AUA GAA Ser Pro Ala Ser Asn Gln Val Met Pro Cys Glu Pro Ile Ile Ile Glu 45 50 55 | 196 | | | | | | | | | | | | | |
| AGG AAC AUA ACA GAG AUA GUG UAU UUG AAU AAC ACC ACC AUA GAG AAA Arg Asn Ile Thr Glu Ile Val Tyr Leu Asn Asn Thr Thr Ile Glu Lys 60 65 70 75 | 244 | | | | | | | | | | | | | |
| GAG AUU UGC CCC GAA GUA GUG GGA UAC AGA AAU UGG UCA AAG CCG CAA Glu Ile Cys Pro Glu Val Val Gly Tyr Arg Asn Trp Ser Lys Pro Gln 80 85 90 | 292 | | | | | | | | | | | | | |
| UGU CAA AUU ACA GGA UUU GCA CCU UUU UCU AAG GAC AAU UCA AUC CGG Cys Gln Ile Thr Gly Phe Ala Pro Phe Ser Lys Asp Asn Ser Ile Arg 95 100 105 | 340 | | | | | | | | | | | | | |
| CUU UCU GCU GGU GGG GAC AUU UGG GUG ACG AGA GAA CCU UAU GUG UCA Leu Ser Ala Gly Gly Asp Ile Trp Val Thr Arg Glu Pro Tyr Val Ser 110 115 120 | 388 | | | | | | | | | | | | | |
| UGC GAC CCU GGC AAG UGU UAU CAA UUU GCA CUC GGG CAG GGG ACC ACA Cys Asp Pro Gly Lys Cys Tyr Gln Phe Ala Leu Gly Gln Gly Thr Thr 125 | ·436 | | | | | | | | | | | | | |
| CUA GAC AAC AAA CAU UCA AAU GGC ACA AUA CAU GAU AGA AUC CCU CAU Leu Asp Asn Lys His Ser Asn Gly Thr Ile His Asp Arg Ile Pro His 140 150 155 | 484 | | | | | | | | | | | | | |
| CGA ACC CUA UUA AUG AAU GAG UUG GGU GUU CCA UUU CAU UUA GGA ACC Arg Thr Leu Leu Met Asn Glu Leu Gly Val Pro Phe His Leu Gly Thr 160 165 170 | 532 | | | | | | | | | | | | | |
| AAA CAA GUG UGU GCA GCA UGG UCC AGC UCA AGU UGU CAC GAU GGA AAA Lys Gln Val Cys Ala Ala Trp Ser Ser Ser Ser Cys His Asp Gly Lys 175 180 185 | 580 | | | | | | | | | | | | | |

| | | | | | | | ACU Thr | | 628 |
|--|--|--|--|--|--|--|--------------------|------------|------|
| | | | | | | | UGG Trp | | 676 |
| | | | | | | | AAU Asn | | 724 |
| | | | | | | | GCU A1 a 250 | | 772 |
| | | | | | | | GGC Gly | CCA Pro | 820 |
| | | | | | | | CCU Pro | CGA Arg | 868 |
| | | | | | | | UCU Ser | | 916 |
| | | | | | | | UCC Ser | | 964 |
| | | | | | | | GAC Asp 330 | | 1012 |
| | | | | | | | AAU Asn | | 1060 |
| | | | | | | | AUG Met | | 1108 |
| | | | | | | | AAA Lys | | 1156 |
| | | | | | | | AGA Arg | | 1204 |
| | | | | | | | UUC Phe 410 | | 1252 |

a

| | | | | | | | | | 100 | | | | | | | | |
|-----------------------------|-----------|-------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-------------------|-----------|-----------|---|------|
| | | | | | | | | | | | | | GAG Glu 425 | | | | 1300 |
| | | | | | | | | | | | | | AAC Asn | | | | 1348 |
| | | | | | | | | | | | | | UCA Ser | | | • | 1396 |
| | | GCG Ala | | | | | | | | UAA | CGUU | JCG (| CAAUI | JUUA(| GA | | 1446 |
| AAA | AAACI | ucc ı | JUGUL | JUCU | AC U | | | | | | | | | | | | 1467 |
| | | | | | | | | | | | | | | | | | |
| (2) | INF | ORMA [*] | rion | FOR | SEQ | ID ! | 10:38 | 3: | | | | | | | | | |
| | | (i) : | SEQUE | ENCE | CHAI | RACTI | ERIS | TICS | : | | | | | | | | |
| (A) LENGTH: 469 amino acids | | | | | | | | | | | | | | | | | |
| (B) TYPE: amino acid | | | | | | | | | | | | | | | | | |
| | | | (D) | тоі | POLO | GY: | linea | ar | | | | | | | | | |
| (ii) MOLECULE TYPE: protein | | | | | | | | | | | | | | | | | |
| | (: | xi) : | SEQUE | ENCE | DESC | CRIP | ΓΙΟΝ: | : SE | Q ID | NO:3 | 38: | | | | | | |
| Met 1 | | Pro | Asn | | | | | Thr | | | | | Ser | Leu 15 | Thr | | |
| Ile | Ala | Thr | Va1 20 | Cys | Phe | Leu | Met | G1n 25 | Ile | Ala | Ile | Leu | Ala 30 | Thr | Thr | | |
| Val | Thr | Leu 35 | His | Leu | Lys | G1 n | His 40 | Glu | Cys | Asp | Ser | Pro 45 | Ala | Ser | Asn | | 2 |
| Gln | Va1 50 | Met | Pro | Cys | Glu | Pro 55 | Ile | Ile | Ile | G1 u | Arg 60 | Asn | Ile | Thr | Glu | | ` |
| Ile 65 | Val | Tyr | Leu | Asn | Asn 70 | Thr | Thr | Ile | Glu | Lys 75 | Glu | Ile | Cys | Pro | G1u 80 | | |
| Val | Val | Gly | Tyr | Arg 85 | Asn | Trp | Ser | Lys | Pro 90 | G1 n | Cys | Gln | Ile | Thr 95 | Gly | | |

Phe Ala Pro Phe Ser Lys Asp Asn Ser Ile Arg Leu Ser Ala Gly Gly

| | | | | | | | | - | 100 | - | | | | | |
|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|-----------------|
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Asp | Ile | Trp 115 | Val | Thr | Arg | Glu | Pro 120 | Tyr | Val | Ser | Cys | Asp 125 | Pro | Gly | Lys |
| Cys | Tyr 130 | Gln | Phe | Ala | Leu | Gly 135 | Gln | G1y | Thr | Thr | Leu 140 | Asp | Asn | Lys | His |
| Ser 145 | Asn | Gly | Thr | Ile | His 150 | Asp | Arg | Ile | Pro | His 155 | Arg | Thr | Leu | Leu | Me1 160 |
| Asn | G1 u | Leu | Gly | Val 165 | Pro | Phe | His | Leu | Gly 170 | Thr | Lys | Gln | Val | Cys 175 | Ala |
| Ala | Trp | Ser | Ser 180 | Ser | Ser | Cys | His | Asp 185 | Gly | Lys | Ala | Trp | Leu 190 | His | Va |
| Cys | Val | Thr 195 | Gly | Asp | Asp | Arg | Asn 200 | Ala | Thr | Ala | Ser | Phe 205 | Ile | Tyr | Ası |
| Gly | Lys 210 | Leu | Val | Asp | Ser | Ile 215 | G1 <i>y</i> | Ser | Trp | Ser | G1n 220 | Asn | Val | Leu | Arg |
| Thr 225 | G1n | Glu | Ser | G1 u | Cys 230 | Val | Cys | Ile | Asn | Gly 235 | Thr | Cys | Thr | Val | Va 1 240 |
| Met | Thr | Asp | Gly | Ser 245 | Ala | Ser | Gly | Arg | A1a 250 | Asp | Thr | Arg | Ile | Leu 255 | Phe |
| Ile | Lys | G1 u | Gly 260 | Lys | Ile | Val | His | Ile 265 | G1y | Pro | Leu | Ser | Gly 270 | Ser | Ala |
| Gln | His | Val 275 | Glu | Glu | Cys | Ser | Cys 280 | Tyr | Pro | Arg | Tyr | Pro 285 | Asp | Val | Arg |
| Cys | Ile 290 | Cys | Arg | Asp | Asn | Trp 295 | Lys | G1y | Ser | Asn | Arg 300 | Pro | Va1 | Ile | Asp |
| Ile 305 | Asn | Met | Glu | Asp | Tyr 310 | Ser | Ile | Asp | Ser | Ser 315 | Tyr | Va1 | Cys | Ser | G1 ₃ |
| Leu | Va1 | G1 y | Asp | Thr 325 | Pro | Arg | Asn | Asp | Asp 330 | Ser | Ser | Ser | Asn | Ser 335 | Asr |
| Cys | Arg | Asp | Pro 340 | Asn | Asn | G1u | Arg | G1y 345 | Asn | Pro | Gly | Val | Lys 350 | G1y | Trp |
| Ala | Phe | Asp 355 | Asn | G1y | Asp | Asp | Va1 360 | Trp | Met | Gly | Arg | Thr 365 | Ile | Ser | Lys |
| Asp | Leu 370 | Arg | Ser | Gly | Tyr | G1u 375 | Thr | Phe | Lys | Val | Ile 380 | Gly | Gly | Trp | Ser |

Thr Pro Asn Ser Lys Ser Gln Val Asn Arg Gln Val Ile Val Asp Asn 385 390395

Asn Asn Trp Ser Gly Tyr Ser Gly Ile Phe Ser Val Glu Gly Lys Ser 405 410 415

Cys Ile Asn Arg Cys Phe Tyr Val Glu Leu Ile Arg Gly Arg Pro Gln 420 425 430

Glu Thr Arg Val Trp Trp Thr Ser Asn Ser Ile Val Val Phe Cys Gly
435 440 445

Thr Ser Gly Thr Tyr Gly Thr Gly Ser Trp Pro Asp Gly Ala Asn Ile 450 455 460

Asn Phe Met Pro Ile 465

(2) INFORMATION FOR SEQ ID NO:39:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1566 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: RNA (genomic)
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Influenza virus
 - (B) STRAIN: wild type A/Ann Arbor/6/60 (H2N2) Egg Passage 2(3)

(vii) IMMEDIATE SOURCE:

(B) CLONE: NP

(ix) FEATURE:

- (A) NAME/KEY: mutation
- (B) LOCATION: replace(113, "a")
- (D) OTHER INFORMATION: /note= "c in ca "master" strain; a in wt2(3); c in 1988 reported wild type E28-32 strain (manuscript) but a in 1988 reported wild type E28-32 strain

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/citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(146, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(627, "c")
- (D) OTHER INFORMATION: /note= "c in ca "master" strain and in wt2(3); a in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(909, "g")
- (D) OTHER INFORMATION: /note= "g in ca "master" strain and in wt2(3); c in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

- (A) NAME/KEY: conflict
- (B) LOCATION: replace(1550, "a")
- (D) OTHER INFORMATION: /note= "a in ca "master" strain and in wt2(3); deletion in 1988 reported wild type E28-32 strain" /citation= ([1][2])

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 46..1539

(D) OTHER INFORMATION: /product= "Nucleoprotein"

/gene= "NP"

/note= "nucleoprotein"
/citation= ([1][2])

(x) PUBLICATION INFORMATION:

(A) AUTHORS: Herlocher, M L Maassab, H F Webster, R W

- (B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus
- (C) JOURNAL: Proceedings of the National Academy of Sciences of the USA
- (G) DATE: 1993
- (K) RELEVANT RESIDUES IN SEQ ID NO:39: FROM 1 TO 1566

(x) PUBLICATION INFORMATION:

(A) AUTHORS: Cox, N J
Kitame, F
Kendal, A P
Maassab, H F
Naeve, C

- (B) TITLE: Identification of sequence changes in the cold-adapted live attenuated influenza vaccine strain, A/Ann Arbor/6/60 (H2N2)
- (C) JOURNAL: Virology
- (D) VOLUME: 167
- (F) PAGES: 554-567
- (G) DATE: 1988
- (K) RELEVANT RESIDUES IN SEQ ID NO:39: FROM 1 TO 1566
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

| | | | | | | Thr | | GAA Glu | | 102 |
|---|--|--|----|--|--|-----|--|-------------------|--|------|
| 5 | | | 10 | | | 15 | | | | |
| | | | | | | | | GGU Gly | | 150 |
| | | | | | | | | AGU Ser 50 | | 198 |
| | | | | | | | | AUG Met | | 246 |
| | | | | | | | | CAU His | | 294 |
| | | | | | | | | AAG Lys | | 342 |
| | | | | | | | | GAA Glu | | 390 |
| | | | | | | | | ACA Thr 130 | | 438 |
| | | | | | | | | ACA Thr | | 486 |
| | | | | | | | | AGG Arg | | 534 |
| | | | | | | | | GCC Ala | | .582 |
| | | | | | | | | AUC Ile | | 630 |
| | | | | | | | | GAG Glu 210 | | 678 |
| | | | | | | | | CUC Leu | | 726 |

| | | | | | | | GUG Val | 774 |
|--|--|--|--|--|--|--|---------------------------|------|
| | | | | | | | UUU Phe | 822 |
| | | | | | | | UCU Ser | 870 |
| | | | | | | | GAC Asp 290 | 918 |
| | | | | | | | CUG Leu | 966 |
| | | | | | | | CCA Pro | 1014 |
| | | | | | | | UUU Phe | 1062 |
| | | | | | | | CCA Pro | 1110 |
| | | | | | | | AAC Asn 370 | 1158 |
| | | | | | | | UGG Trp | 1206 |
| | | | | | | | UCU Ser | 1254 |
| | | | | | | | CUC Leu | 1302 |
| | | | | | | | GAG Glu | 1350 |
| | | | | | | | GGU G1 <i>y</i> 450 | 1398 |

W

| | | | | | UCC Ser | | | | | | | 1446 |
|------|------|-------|-------|-----|------------|-------|----|--|--|--|--|------|
| | | | | | AAC Asn | | | | | | | 1494 |
| | | | | | UUC Phe | | | | | | | 1539 |
| JAA(| GAAA | AAA A | NUACO | CUU | SU UL | JCUAC | ะบ | | | | | 1566 |

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 498 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

Met Ala Ser Gln Gly Thr Lys Arg Ser Tyr Glu Gln Met Glu Thr Asp 1 5 10 15

Gly Glu Arg Gln Asn Ala Asn Glu Ile Arg Ala Ser Val Gly Lys Met 20 25 30

Ile Gly Gly Ile Gly Arg Phe Tyr Ile Gln Met Cys Thr Glu Leu Lys 35 40 45

Leu Ser Asp Tyr Glu Gly Arg Leu Ile Gln Asn Ser Leu Thr Ile Glu 50 55 60

Arg Met Val Leu Ser Ala Phe Asp Glu Arg Arg Asn Lys Tyr Leu Glu 65 70 75 80

Glu His Pro Ser Ala Gly Lys Asp Pro Lys Lys Thr Gly Gly Pro Ile 85 90 95

Tyr Lys Arg Val Asp Gly Lys Trp Met Arg Glu Leu Val Leu Tyr Asp 100 105 110

Lys Glu Glu Ile Arg Arg Ile Trp Arg Gln Ala Asn Asn Gly Asp Asp 115 120 125

W

Ala Thr Ala Gly Leu Thr His Met Met Ile Trp His Ser Asn Leu Asn Asp Thr Thr Tyr Gln Arg Thr Arg Ala Leu Val Arg Thr Gly Met Asp Pro Arg Met Cys Ser Leu Met Gln Gly Ser Thr Leu Pro Arg Arg Ser 170 Gly Ala Ala Gly Ala Ala Val Lys Gly Val Gly Thr Met Val Met Glu 180 Leu Ile Arg Met Ile Lys Arg Gly Ile Asn Asp Arg Asn Phe Trp Arg Gly Glu Asn Gly Arg Lys Thr Arg Asn Ala Tyr Glu Arg Met Cys Asn 215 Ile Leu Lys Gly Lys Phe Gln Thr Ala Ala Gln Arg Ala Met Met Asp 240 225 · 230 Gln Val Arg Glu Ser Arg Asn Pro Gly Asn Ala Glu Ile Glu Asp Leu Ile Phe Leu Ala Arg Ser Ala Leu Ile Leu Arg Gly Ser Val Ala His 270 Lys Ser Cys Leu Pro Ala Cys Val Tyr Gly Pro Ala Val Ala Ser Gly Tyr Asp Phe Glu Lys Glu Gly Tyr Ser Leu Val Gly Ile Asp Pro Phe Lys Leu Leu Gln Asn Ser Gln Val Tyr Ser Leu Ile Arg Pro Asn Glu 305 310 315 320 Asn Pro Ala His Lys Ser Gln Leu Val Trp Met Ala Cys Asn Ser Ala 325 330 Ala Phe Glu Asp Leu Arg Val Ser Ser Phe Ile Arg Gly Thr Lys Val 345 Ile Pro Arg Gly Lys Leu Ser Thr Arg Gly Val Gln Ile Ala Ser Asn 355 Glu Asn Met Asp Thr Met Gly Ser Ser Thr Leu Glu Leu Arg Ser Arg 380 Tyr Trp Ala Ile Arg Thr Arg Ser Gly Gly Asn Thr Asn Gln Gln Arg 390 395 Ala Ser Ala Gly Gln Ile Ser Val Gln Pro Thr Phe Ser Val Gln Arg 405 415 Asn Leu Pro Phe Asp Lys Pro Thr Ile Met Ala Ala Phe Thr Gly Asn

M

420

430

Ala Glu Gly Arg Thr Ser Asp Met Arg Ala Glu Ile Ile Arg Met Met 435 440 445

425

Glu Gly Ala Lys Pro Glu Glu Val Ser Phe Gln Gly Arg Gly Val Phe 450 455 460

Glu Leu Ser Asp Glu Lys Ala Thr Asn Pro Ile Val Pro Ser Phe Asp 465 470 475 480

Met Ser Asn Glu Gly Ser Tyr Phe Phe Gly Asp Asn Ala Glu Glu Tyr 485 490 495

Asp Asn

 $\mathcal{N}/$